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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 : A61K 37/02, 39/12, C12Q 1/70, G01N 33/53 — A1

(11) International Publication Number: WO 94/28920

(43) International Publication Date: 22 December 1994 (22.12.94)

(21) International Application Number: PCT/US94/05739

(22) International Filing Date: 7 June 1994 (07.06.94)

(30) Priority Data:
073,028 7 June 1993 (07.06.93) US

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(81) Designated States: AU, BB, BG, BR, BY, CA, CN, CZ, FI, GE, HU, JP, KG, KR, KZ, LK, LV, MD, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, UA, UZ, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: SYNTHETIC PEPTIDE INHIBITORS OF HIV TRANSMISSION

(57) Abstract

The present invention relates to peptides which exhibit potent anti-retroviral activity. The peptides of the invention comprise DP-178 (SEQ ID:1) peptide corresponding to amino acids 638 to 673 of the HIV-1_{LAI} gp41 protein, and fragments, analogs and homologs of DP-178. The invention further relates to the uses of such peptides as inhibitory of human and non-human retroviral, especially HIV, transmission to uninfected cells.

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SYNTHETIC PEPTIDE INHIBITORS OF HIV TRANSMISSION

1. INTRODUCTION

The present invention relates to DP-178 (SEQ ID:1), a peptide corresponding to amino acids 638 to 673 of the HIV-1_{LAI} transmembrane protein (TM) gp41, and portions, analogs, and homologs of DP-178 (SEQ ID:1), all of which exhibit anti-viral activity. Such anti-viral activity includes, but is not limited to, the inhibition of HIV transmission to uninfected CD-4^+ cells. Further, the invention relates to the use of DP-178 (SEQ ID:1) and DP-178 fragments and/or analogs or homologs as inhibitors of human and non-human retroviral, especially HIV, transmission to uninfected cells. Still further, the invention relates to the use of DP-178 as a HIV subtype-specific diagnostic. The present invention also relates to antiviral peptides analogous to DP-107, a peptide corresponding to amino acids 558 to 595 of the HIV-1_{LAI} transmembrane protein (TM) gp41, that are present in other enveloped viruses. The present invention further relates to methods for identifying antiviral compounds that disrupt the interaction between DP-178 and DP-107, and/or between DP-107-like and DP-178-like peptides. The invention is demonstrated by way of a working example wherein DP-178 (SEQ ID:1), and a peptide whose sequence is homologous to DP-178 are each shown to be potent, non-cytotoxic inhibitors of HIV-1 transfer to uninfected CD-4^+ cells. The invention is further demonstrated by working examples wherein peptides having antiviral and/or structural similarity to DP-107 and DP-178 are identified.

2. BACKGROUND OF THE INVENTION

2.1. THE HUMAN IMMUNODEFICIENCY VIRUS

The human immunodeficiency virus (HIV) has been implicated as the primary cause of the slowly degenerative immune system disease termed acquired immune deficiency syndrome (AIDS) (Barre-Sinoussi, F. et al., 1983, Science 220:868-870; Gallo, R. et al., 1984, Science 224:500-503). there are at least two distinct types of HIV: HIV-1 (Barre-Sinoussi, F. et al., 1983, Science 220:868-870; Gallo R. et al., 1984, Science 224:500-503) and HIV-2 (Clavel, F. et al., 1986, Science 233:343-346; Guyader, M. et al., 1987, Nature 326:662-669). Further, a large amount of genetic heterogeneity exists within populations of each of these types. Infection of human CD-4$^+$ T-lymphocytes with an HIV virus leads to depletion of the cell type and eventually to opportunistic infections, neurological dysfunctions, neoplastic growth, and ultimately death.

HIV is a member of the lentivirus family of retroviruses (Teich, N. et al., 1984, RNA Tumor Viruses, Weiss, R. et al., eds., CSH-Press, pp. 949-956). Retroviruses are small enveloped viruses that contain a diploid, single-stranded RNA genome, and replicate via a DNA intermediate produced by a virally-encoded reverse transcriptase, an RNA-dependent DNA polymerase (Varmus, H., 1988, Science 240:1427-1439). Other retroviruses include, for example, oncogenic viruses such as human T-cell leukemia viruses (HTLV-I,-II,-III), and feline leukemia virus.

The HIV viral particle consists of a viral core, composed of capsid proteins, that contains the viral RNA genome and those enzymes required for early replicative events. Myristylated Gag protein forms an

outer viral shell around the viral core, which is, in turn, surrounded by a lipid membrane envelope derived from the infected cell membrane. The HIV envelope surface glycoproteins are synthesized as a single 160 Kd precursor protein which is cleaved by a cellular protease during viral budding into two glycoproteins, gp41 and gp120. gp41 is a transmembrane protein and gp120 is an extracellular protein which remains non-covalently associated with gp41, possibly in a trimeric or multimeric form (Hammarskjold, M. and Rekosh, D., 1989, Biochem. Biophys. Acta 989:269-280).

HIV is targeted to CD-4$^+$ cells because the CD-4 cell surface protein acts as the cellular receptor for the HIV-1 virus (Dalgleish, A. et al., 1984, Nature 312:763-767; Klatzmann et al., 1984, Nature 312:767-768; Maddon et al., 1986, Cell 47:333-348). Viral entry into cells is dependent upon gp120 binding the cellular CD-4$^+$ receptor molecules (McDougal, J.S. et al., 1986, Science 231:382-385; Maddon, P.J. et al., 1986, Cell 47:333-348) and thus explains HIV's tropism for CD-4$^+$ cells, while gp41 anchors the envelope glycoprotein complex in the viral membrane.

2.2. HIV TREATMENT

HIV infection is pandemic and HIV associated diseases represent a major world health problem. Although considerable effort is being put into the successful design of effective therapeutics, currently no curative anti-retroviral drugs against AIDS exist. In attempts to develop such drugs, several stages of the HIV life cycle have been considered as targets for therapeutic intervention (Mitsuya, H. et al., 1991, FASEB J. 5:2369-2381). For example, virally encoded reverse transcriptase has been one focus of drug development. A number of reverse-transcriptase-

targeted drugs, including 2',3'-dideoxynucleoside analogs such as AZT, ddI, ddC, and d4T have been developed which have been shown to been active against HIV (Mitsuya, H. et al., 1991, Science 249:1533-1544). While beneficial, these nucleoside analogs are not curative, probably due to the rapid appearance of drug resistant HIV mutants (Lander, B. et al., 1989, Science 243:1731-1734). In addition, the drugs often exhibit toxic side effects such as bone marrow suppression, vomiting, and liver function abnormalities.

Attempts are also being made to develop drugs which can inhibit viral entry into the cell, the earliest stage of HIV infection. Here, the focus has thus far been on CD4, the cell surface receptor for HIV. Recombinant soluble CD4, for example, has been shown to inhibit infection of CD-4$^+$ T-cells by some HIV-1 strains (Smith, D.H. et al., 1987, Science 238:1704-1707). Certain primary HIV-1 isolates, however, are relatively less sensitive to inhibition by recombinant CD-4 (Daar, E. et al., 1990, Proc. Natl. Acad. Sci. USA 87:6574-6579). In addition, recombinant soluble CD-4 clinical trials have produced inconclusive results (Schooley, R. et al., 1990, Ann. Int. Med. 112:247-253; Kahn, J.O. et al., 1990, Ann. Int. Med. 112:254-261; Yarchoan, R. et al., 1989, Proc. Vth Int. Conf. on AIDS, p. 564, MCP 137).

The late stages of HIV replication, which involve crucial virus-specific secondary processing of certain viral proteins, have also been suggested as possible anti-HIV drug targets. Late stage processing is dependent on the activity of a viral protease, and drugs are being developed which inhibit this protease (Erickson, J., 1990, Science 249:527-533). The

clinical outcome of these candidate drugs is still in question.

Attention is also being given to the development of vaccines for the treatment of HIV infection. The HIV-1 envelope proteins (gp160, gp120, gp41) have been shown to be the major antigens for anti-HIV antibodies present in AIDS patients (Barin, et al., 1985, Science 228:1094-1096). Thus far, therefore, these proteins seem to be the most promising candidates to act as antigens for anti-HIV vaccine development. To this end, several groups have begun to use various portions of gp160, gp120, and/or gp41 as immunogenic targets for the host immune system. See for example, Ivanoff, L. et al., U.S. Pat. No. 5,141,867; Saith, G. et al., WO 92/22,654; Shafferman, A., WO 91/09,872; Formoso, C. et al., WO 90/07,119. Clinical results concerning these candidate vaccines, however, still remain far in the future.

Thus, although a great deal of effort is being directed to the design and testing of anti-retroviral drugs, a truly effective, non-toxic treatment is still needed.

3. SUMMARY OF THE INVENTION

The present invention relates to DP-178 (SEQ ID:1), a 36-amino acid synthetic peptide corresponding to amino acids 638 to 673 of the transmembrane protein (TM) gp41 from the HIV-1 isolate LAI, which exhibits potent anti-HIV-1 activity. As evidenced by the example presented below, in Section 6, the DP-178 (SEQ ID:1) anti-viral activity is so high that, on a weight basis, no other known anti-HIV agent is effective at concentrations as low as those at which DP-178 (SEQ ID:1) exhibits its inhibitory effects. The invention further relates to those portions, analogs, and

homologs of DP-178 which also show such antiviral activity. The antiviral activity of such DP-178 portions, analogs, and homologs, includes, but is not limited to the inhibition of HIV transmission to uninfected CD-4$^+$ cells. The invention relates to the use of DP-178 (SEQ ID:1) and DP-178 fragments and/or analogs or homologs. Such uses may include, but are not limited to, the use of the peptides as inhibitors of human and non-human retroviral, especially HIV, transmission to uninfected cells, and as type and/or subtype-specific diagnostic tools.

An embodiment of the invention is demonstrated below wherein an extremely low concentration of DP-178 (SEQ ID:1), and very low concentrations of a DP-178 homolog (SEQ ID:3) are shown to be potent inhibitors of HIV-1 mediated CD-4$^+$ cell-cell fusion (i.e., syncytial formation) and infection of CD-4$^+$ cells by cell-free virus. Further, it is shown that DP-178 (SEQ ID:1) is not toxic to cells, even at concentrations 3 logs higher than the inhibitory DP-178 (SEQ ID:1) concentration.

The invention also relates to analogous DP178 peptides in other enveloped viruses that demonstrate similar antiviral properties.

The invention further relates to peptides analogous to DP-107, a peptide corresponding to amino acids 558-595 of the HIV-1_{LAI} transmembrane protein (TM) of gp41, that are present in other enveloped viruses, and demonstrate antiviral properties. The present invention is based, in part, on the surprising discovery that the DP-107 and DP-108 domains of the gp41 protein non-covalently complex with each other, and that their interaction is necessary for the normal activity of the virus. The invention, therefore, further relates to methods for identifying antiviral

compounds that disrupt the interaction between DP-107 and DP-178, and/or between DP-107-like and DP-178-like peptides.

Embodiments of the invention are demonstrated, below, wherein peptides having structural and/or similarity to DP-107 and DP-178 are identified.

3.1. DEFINITIONS

Peptides are defined herein as organic compounds comprising two or more amino acids covalently joined by peptide bonds. Peptides may be referred to with respect to the number of constituent amino acids, i.e., a dipeptide contains two amino acid residues, a tripeptide contains three, etc. Peptides containing ten or fewer amino acids may be referred to as oligopeptides, while those with more than ten amino acid residues are polypeptides.

Peptide sequences defined herein are represented by one-letter symbols for amino acid residues as follows:

A (alanine)
R (arginine)
N (asparagine)
D (aspartic acid)
C (cysteine)
Q (glutamine)
E (glutamic acid)
G (glycine)
H (histidine)
I (isoleucine)
L (leucine)
K (lysine)
M (methionine)
F (phenylalanine)
P (proline)

S (serine)
T (threonine)
W (tryptophan)
Y (tyrosine)
V (valine)

4. BRIEF DESCRIPTION OF THE FIGURES

FIG. 1. Amino acid sequence of DP-178 (SEQ ID:1) derived from HIV_{LAI}; DP-178 homologs derived from $HIV\text{-}1_{SF2}$ (DP-185; SEQ ID:3), $HIV\text{-}1_{RF}$ (SEQ ID:4), and $HIV\text{-}1_{MN}$ (SEQ ID:5); DP-178 homologs derived from amino acid sequences of two prototypic HIV-2 isolates, namely, $HIV\text{-}2_{rod}$ (SEQ ID:6) and $HIV\text{-}2_{NIHZ}$ (SEQ ID:7); control peptides: DP-180 (SEQ ID:2), a peptide incorporating the amino acid residues of DP-178 in a scrambled sequence; DP-118 (SEQ ID:10) unrelated to DP-178, which inhibits HIV-1 cell free virus infection; DP-125 (SEQ ID:8), unrelated to DP-178, was also previously shown to inhibit HIV-1 cell free virus infection (Wild et al., 1992, Proc. Natl. Acad. Sci USA 89:10,537-10,541); DP-116 (SEQ ID:9), unrelated to DP-178 had previously been shown to be negative for inhibition of HIV-1 infection using the cell-free virus infection assay (Wild, et al., 1992, Proc. Natl. Acad. Sci USA 89:10,537-10,541). Throughout the figures, the one letter amino acid code is used.

FIG. 2. Inhibition of HIV-1 cell-free virus infection by synthetic peptides. IC50 refers to the concentration of peptide that inhibits RT production from infected cells by 50% compared to the untreated control. Control: the level of RT produced by untreated cell cultures infected with the same level of virus as treated cultures.

FIG. 3. Inhibition of HIV-1 and HIV-2 cell-free virus infection by the synthetic peptide DP-178 (SEQ

ID:1). IC50: concentration of peptide that inhibits RT production by 50% compared to the untreated control. Control: Level of RT produced by untreated cell cultures infected with the same level of virus as treated cultures.

FIG. 4A. Fusion Inhibition Assay. DP-178 (SEQ ID:1) inhibition of HIV-1 prototypic isolate-mediated syncytia formation. Data represents the number of virus-induced syncytia per cell.

FIG. 4B. Fusion Inhibition Assay. DP-180 (SEQ ID:2): scrambled control peptide. DP-185 (SEQ ID:3): DP-178 homolog derived from HIV-1_{SF2} isolate. Control: number of syncytia produced in the absence of peptide.

FIG. 5. Fusion inhibition assay: HIV-1 vs. HIV-2. Data represents the number of virus-induced syncytia per well. ND: not done.

FIG. 6. Cytotoxicity study of DP-178 (SEQ ID:1) and DP-116 (SEQ ID:9) on CEM cells. Cell proliferation data is shown.

FIG. 7. Schematic representation of HIV-gp41 and maltose binding protein (MBP)-gp41 fusion proteins. DP107 and DP178 are synthetic peptides based on the two putative helices of gp41. The letter P in the DP107 boxes denotes an Ile to Pro mutation at amino acid number 578. Amino acid residues are numbered according to Meyers et al., Human Retroviruses and AIDS, 1991, Theoret. Biol. and Biophys. Group, Los Alamos Natl. Lab., Los Alamos, NM.

FIG. 8. A point mutation alters the conformation and anti-HIV activity of M41.

FIG. 9. Abrogation of DP178 anti-HIV activity. Cell fusion assays were carried out in the presence of 10 nM DP178 and various concentrations of M41Δ178 or M41PΔ178.

FIG. 10. Binding of DP178 to leucine zipper of gp41 analyzed by ELISA.

FIG. 11A-B. Models for a structural transition in the HIV-1 TM protein. Two models are proposed which indicate a structural transition from a native oligomer to a fusogenic state following a trigger event (possibly gp120 binding to CD4). Common features of both models include (1) the native state is held together by noncovalent protein-protein interactions to form the heterodimer of gp120/41 and other interactions, principally though gp41 interactive sites, to form homo-oligomers on the virus surface of the gp120/41 complexes; (2) shielding of the hydrophobic fusogenic peptide at the N-terminus (F) in the native state; and (3) the leucine zipper domain (DP107) exists as a homo-oligomer coiled coil only in the fusogenic state. The major differences in the two models include the structural state (native or fusogenic) in which the DP107 and DP178 domains are complexed to each other. In the first model (A; FIG. 11A) this interaction occurs in the native state and in B during the fusogenic state. When triggered, the fusion complex in the model depicted in (A) is generated through formation of coiled-coil interactions in homologous DP107 domains resulting in an extended α-helix. This conformational change positions the fusion peptide for interaction with the cell membrane. In the second model (B; FIG. 11B), the fusogenic complex is stabilized by the association of the DP178 domain with the DP107 coiled-coil.

FIG. 12. Motif design using heptad repeat positioning of amino acids of known coiled-coils.

FIG. 13. Motif design using proposed heptad repeat positioning of amino acids of DP-107 and DP-178.

FIG. 14. Hybrid motif design crossing GCN4 and DP-107.

FIG. 15. Hybrid motif design crossing GCN4 and DP-178.

FIG. 16. Hybrid motif design 107x178x4, crossing DP-107 and DP-178. This motif was found to be the most consistent at identifying relevant DP-107-like and DP-178-like peptide regions.

FIG. 17. Hybrid motif design ALLMOTI5, crossing GCN4, DP-107, and DP-178.

FIG. 18. Hybrid motif design crossing GCN4, DP-107, DP-178, c-Fos c-Jun, c-Myc, and Flu Loop 36.

FIG. 19. Motifs designed to identify N-terminal proline-leucine zipper motifs.

FIG. 20. Search results for HIV-1 (BRU isolate) envelope protein gp41. Sequence search motif designations: Spades (♠): 107x178x4; Hearts (♥) ALLMOTI5; Clubs (♣): PLZIP; Diamonds (♦): transmembrane region (the putative transmembrane domains were identified using a PC/Gene program designed to search for such peptide regions). Asterisk (*): Lupas method. The amino acid sequences identified by each motif are bracketed by the respective characters. Representative sequences chosen based on all searches are underlined and in bold. DP-107 and DP-178 sequences are marked, and additionally double-underlined and italicized.

FIG. 21. Search results for human respiratory syncytial virus (RSV) strain A2 fusion glycoprotein F1. Sequence search motif designations are as in FIG. 20.

FIG. 22. Search results for simian immunodeficiency virus (SIV) envelope protein gp41 (AGM3 isolate). Sequence search motif designations are as in FIG. 20.

FIG. 23. Search results for canine distemper virus (strain Onderstepoort) fusion glycoprotein 1. Sequence search motif designations are as in FIG. 20.

FIG. 24. Search results for newcastle disease virus (strain Australia-Victoria/32) fusion glycoprotein F1. Sequence search motif designations are as in FIG. 20.

FIG. 25. Search results for human parainfluenza 3 virus (strain NIH 47885) fusion glycoprotein F1. Sequence search motif designations are as in FIG. 20.

FIG. 26. Search results for influenza A virus (strain A/AICHI/2/68) hemagglutinin precursor HA2. Sequence search designations are as in FIG. 20.

FIG. 27. Coiled-coil structural similarity and anti-RSV antiviral activity of 35-mer peptides synthesized utilizing the sequence of a 48-amino acid RSV F2 peptide which spans sequences identified utilizing the computer-assisted searches described herein. For the exact location and motifs utilized, see FIG. 21. "+" symbols are relative indicators of either structural similarity or antiviral activity, with a greater number of "+" symbols indicating a higher relative similarity or antiviral activity.

FIG. 28. Coiled-coil structural similarity and anti-RSV antiviral activity of 35-mer peptides synthesized utilizing the sequence of a 53-amino acid RSV F1 peptide which spans sequences identified utilizing the computer-assisted searches described herein. See FIG. 21 for the exact location and motifs used. "+" symbols are as described for FIG. 27.

FIG. 29. Coiled-coil structural similarity and anti-human parainfluenza 3 virus (HPF3) antiviral activity of 35-mer peptides synthesized utilizing the

sequence of a 56-amino acid HPF3 peptide which spans sequences identified utilizing computer-assisted searches described herein. For the exact location and motifs utilized, see FIG. 25. "+" symbols are as described in FIG. 27.

FIG. 30. Coiled-coil structural similarity and anti-HPF3 antiviral activity of 35-mer peptides synthesized utilizing the sequence of a 70-amino acid HPF3 peptide which spans sequences identified utilizing the computer-assisted searches described herein. For the exact location and motifs utilized, see FIG. 25. "+" symbols are as described in FIG. 27.

5. DETAILED DESCRIPTION OF THE INVENTION

Described herein are peptides that exhibit potent antiviral activity. These peptides include DP-178 (SEQ ID:1), a gp41-derived 36 amino acid peptide, fragments and/or analogs of DP-178, and peptides which are homologous to DP-178. In addition, these peptides may include peptides exhibiting anti-viral activity which are analogous to DP-107, a 38 amino acid peptide corresponding to residues 558 to 595 of the HIV-1_{LAI} transmembrane (TM) gp41 protein, and which are present in other enveloped viral proteins. Also described here are assays for testing the antiviral activities of such peptides. The present invention is based, in part, of the surprising discovery that the DP-107 and DP-178 domains of the gp41 protein complex with each other via non-covalent protein-protein interactions which are necessary for normal activity of the virus. As such, methods are described for the identification of antiviral compounds that disrupt the interaction between DP-107 and DP-178 peptides, and between DP-107-like and DP-178-like peptides. Finally, the use of the peptides of the invention as inhibitors of non-

human and human viral and retroviral, especially HIV, transmission are detailed, as is the use of the peptides as diagnostic indicators of the presence of specific, viruses, especially retroviruses.

While not limited to any theory of operation, the following model is proposed to explain the potent anti-HIV activity of DP178, based, in part, on the experiments described in the working examples, infra. In the viral protein, gp41, DP178 corresponds to a putative α-helix region located in the C-terminal end of the gp41 ectodomain, and appears to associate with a distal site on gp41 whose interactive structure is influenced by the leucine zipper motif, a coiled-coil structure, referred to as DP107. The association of these two domains may reflect a molecular linkage or "molecular clasp" intimately involved in the fusion process. It is of interest that mutations in the C-terminal α-helix motif of gp41 (i.e., the D178 domain) tend to enhance the fusion ability of gp41, whereas mutations in the leucine zipper region (i.e., the DP107 domain) decrease or abolish the fusion ability of the viral protein. It may be that the leucine zipper motif is involved in membrane fusion while the C-terminal α-helix motif serves as a molecular safety to regulate the availability of the leucine zipper during virus-induced membrane fusion.

On the basis of the foregoing, two models are proposed of gp41-mediated membrane fusion which are schematically shown in FIG. 11A-B. The reason for proposing two models is that the temporal nature of the interaction between the regions defined by DP107 and DP178 cannot, as yet, be pinpointed. Each model envisions two conformations for gp41 - one in a "native" state as it might be found on a resting virion. The other in a "fusogenic" state to reflect

conformational changes triggered following binding of gp120 to CD4 and just prior to fusion with the target cell membrane. The strong binding affinity between gp120 and CD4 may actually represent the trigger for the fusion process obviating the need for a pH change such as occurs for viruses that fuse within intracellular vesicles. The two major features of both models are: (1) the leucine zipper sequences (DP107) in each chain of oligomeric envelope are held apart in the native state and are only allowed access to one another in the fusogenic state so as to form the extremely stable coild-coils, and (2) association of the DP178 and DP107 sites as they exist in gp41 occur either in the native or fusogenic state. FIG. 11A depicts DP178/DP107 interaction in the native state as a molecular class. On the other hand, if one assumes that the most stable form of the envelope occurs in the fusogenic state, the model in FIG. 11B can be considered.

When synthesized as peptides, both DP107 and DP178 are potent inhibitors of HIV infection and fusion, probably by virtue of their ability to form complexes with viral gp41 and interfere with its fusogenic process; e.g., during the structural transition of the viral protein from the native structure to the fusogenic state, the DP178 and DP107 peptides may gain access to their respective binding sites on the viral gp41, and exert a disruptive influence. DP107 peptides which demonstrate anti-HIV activity are described in Applicants' co-pending application Serial No. 07/927,532, filed August 7, 1992, which is incorporated by reference herein in its entirety.

As shown in the working examples, infra, a truncated recombinant gp41 protein corresponding the

ectodomain of gp41 containing both DP107 and DP178 domains (excluding the fusion peptide, transmembrane region and cytoplasmic domain of gp41) did not inhibit HIV-1 induced fusion. However, when a single mutation was introduced to disrupt the coiled-coil structure of the DP107 domain -- a mutation which results in a total loss of biological activity of DP107 peptides -- the inactive recombinant protein was transformed to an active inhibitor of HIV-1 induced fusion. This transformation may result from liberation of the potent DP178 domain from a molecular clasp with the leucine zipper, DP107 domain.

For clarity of discussion, the invention will be described for DP178 peptide inhibitors of HIV. However, the principles may be analogously applied to other fusogenic enveloped viruses, including but not limited to those viruses containing the peptides listed in Tables V through X, below.

5.1. DP-178 AND DP-178-LIKE PEPTIDES

The peptide DP-178 (SEQ ID:1) of the invention corresponds to amino acid residues 638 to 673 of the transmembrane protein gp41 from the HIV-1_{LAI} isolate, and has the 36 amino acid sequence (reading from amino to carboxy terminus):

NH_2-YTSLIHSLIEESQNQQEKNEQELLELDKWASLWNWF-COOH (SEQ ID:1)

In addition to the full-length DP-178 (SEQ ID:1) 36-mer, the peptides of the invention may include truncations of the DP-178 (SEQ ID:1) peptide which exhibit antiviral activity. Such truncated DP-178 (SEQ ID:1) peptides may comprise peptides of between 3 and 36 amino acid residues (i.e., peptides ranging in size from a tripeptide to a 36-mer polypeptide), and

may include but are not limited to those listed in Tables I and II, below. Peptide sequences in these tables are listed from amino (left) to carboxy (right) terminus. "X" may represent an amino group ($-NH_2$) and "Z" may represent a carboxyl (-COOH) group. Alternatively, as described below, "X" and/or "Z" may represent a hydrophobic group, an acetyl group, a FMOC group, an amido group, or a covalently attached macromolecule.

TABLE I
DP-178 (SEQ ID:1) CARBOXY TRUNCATIONS

X-YTS-Z
X-YTSL-Z
X-YTSLI-Z
X-YTSLIH-Z
X-YTSLIHS-Z
X-YTSLIHSL-Z
X-YTSLIHSLI-Z
X-YTSLIHSLIE-Z
X-YTSLIHSLIEE-Z
X-YTSLIHSLIEES-Z
X-YTSLIHSLIEESQ-Z
X-YTSLIHSLIEESQN-Z
X-YTSLIHSLIEESQNQ-Z
X-YTSLIHSLIEESQNQQ-Z
X-YTSLIHSLIEESQNQQE-Z
X-YTSLIHSLIEESQNQQEK-Z
X-YTSLIHSLIEESQNQQEKN-Z
X-YTSLIHSLIEESQNQQEKNE-Z
X-YTSLIHSLIEESQNQQEKNEQ-Z
X-YTSLIHSLIEESQNQQEKNEQE-Z
X-YTSLIHSLIEESQNQQEKNEQEL-Z
X-YTSLIHSLIEESQNQQEKNEQELL-Z
X-YTSLIHSLIEESQNQQEKNEQELLE-Z
X-YTSLIHSLIEESQNQQEKNEQELLEL-Z
X-YTSLIHSLIEESQNQQEKNEQELLELD-Z
X-YTSLIHSLIEESQNQQEKNEQELLELDK-Z
X-YTSLIHSLIEESQNQQEKNEQELLELDKW-Z
X-YTSLIHSLIEESQNQQEKNEQELLELDKWA-Z
X-YTSLIHSLIEESQNQQEKNEQELLELDKWAS-Z
X-YTSLIHSLIEESQNQQEKNEQELLELDKWASL-Z
X-YTSLIHSLIEESQNQQEKNEQELLELDKWASLW-Z
X-YTSLIHSLIEESQNQQEKNEQELLELDKWASLWN-Z
X-YTSLIHSLIEESQNQQEKNEQELLELDKWASLWNW-Z
X-YTSLIHSLIEESQNQQEKNEQELLELDKWASLWNWF-Z

The one letter amino acid code is used.

Additionally,

"X" may represent an amino group, a hydrophobic group, including but not limited to carbobenzoxyl, dansyl, or T-butyloxycarbonyl; an acetyl group; a 9-fluorenylmethoxy-carbonyl (FMOC) group; a macromolecular carrier group including but not limited to lipid-fatty acid conjugates, polyethylene glycol, or carbohydrates.

"Z" may represent a carboxyl group; an amido group; a T-butyloxycarbonyl group; a macromolecular carrier group including but not limited to lipid-fatty acid conjugates, polyethylene glycol, or carbohydrates.

TABLE II
DP-178 (SEQ ID:1) AMINO TRUNCATIONS

X-NWF-Z
X-WNWF-Z
X-LWNWF-Z
X-SLWNWF-Z
X-ASLWNWF-Z
X-WASLWNWF-Z
X-KWASLWNWF-Z
X-DKWASLWNWF-Z
X-LDKWASLWNWF-Z
X-ELDKWASLWNWF-Z
X-LELDKWASLWNWF-Z
X-LLELDKWASLWNWF-Z
X-ELLELDKWASLWNWF-Z
X-QELLELDKWASLWNWF-Z
X-EQELLELDKWASLWNWF-Z
X-NEQELLELDKWASLWNWF-Z
X-KNEQELLELDKWASLWNWF-Z
X-EKNEQELLELDKWASLWNWF-Z
X-QEKNEQELLELDKWASLWNWF-Z
X-QQEKNEQELLELDKWASLWNWF-Z
X-NQQEKNEQELLELDKWASLWNWF-Z
X-QNQQEKNEQELLELDKWASLWNWF-Z
X-SQNQQEKNEQELLELDKWASLWNWF-Z
X-ESQNQQEKNEQELLELDKWASLWNWF-Z
X-EESQNQQEKNEQELLELDKWASLWNWF-Z
X-IEESQNQQEKNEQELLELDKWASLWNWF-Z
X-LIEESQNQQEKNEQELLELDKWASLWNWF-Z
X-SLIEESQNQQEKNEQELLELDKWASLWNWF-Z
X-HSLIEESQNQQEKNEQELLELDKWASLWNWF-Z
X-IHSLIEESQNQQEKNEQELLELDKWASLWNWF-Z
X-LIHSLIEESQNQQEKNEQELLELDKWASLWNWF-Z
X-SLIHSLIEESQNQQEKNEQELLELDKWASLWNWF-Z
X-TSLIHSLIEESQNQQEKNEQELLELDKWASLWNWF-Z
X-YTSLIHSLIEESQNQQEKNEQELLELDKWASLWNWF-Z

The one letter amino acid code is used.

Additionally,

"X" may represent an amino group, a hydrophobic group, including but not limited to carbobenzoxyl, dansyl, or T-butyloxycarbonyl; an acetyl group; a 9-fluorenylmethoxy-carbonyl group; a macromolecular carrier group including but not limited to lipid-fatty acid conjugates, polyethylene glycol, or carbohydrates.

"Z" may represent a carboxyl group; an amido group; a T-butyloxycarbonyl group; a macromolecular carrier group including but not limited to lipid-fatty acid conjugates, polyethylene glycol, or carbohydrates.

The antiviral peptides of the invention also include analogs of DP-178 and/or DP-178 truncations which may include, but are not limited to, peptides comprising the DP-178 (SEQ ID:1) sequence, or DP-178 truncated sequence, containing one or more amino acid substitutions, insertions and/or deletions. Analogs of DP-178 homologs, described below, are also within the scope of the invention. The DP-178 analogs of the invention exhibit antiviral activity, and may, further, possess additional advantageous features, such as, for example, increased bioavailability, and/or stability, or reduced host immune recognition.

HIV-1 and HIV-2 envelope proteins are structurally distinct, but there exists a striking amino acid conservation within the DP-178-corresponding regions of HIV-1 and HIV-2. The amino acid conservation is of a periodic nature, suggesting some conservation of structure and/or function. Therefore, one possible class of amino acid substitutions would include those amino acid changes which are predicted to stabilize the structure of the DP-178 peptides of the invention.

Amino acid substitutions may be of a conserved or non-conserved nature. Conserved amino acid substitutions consist of replacing one or more amino acids of the DP-178 (SEQ ID:1) peptide sequence with amino acids of similar charge, size, and/or hydrophobicity characteristics, such as, for example, a glutamic acid (E) to aspartic acid (D) amino acid substitution. When only conserved substitutions are made, the resulting peptide is functionally equivalent to DP-178 (SEQ ID:1) or the DP-178 peptide from which it is derived. Non-conserved substitutions consist of replacing one or more amino acids of the DP-178 (SEQ ID:1) peptide sequence with amino acids possessing dissimilar charge, size, and/or hydrophobicity

characteristics, such as, for example, a glutamic acid (E) to valine (V) substitution.

Amino acid insertions may consist of single amino acid residues or stretches of residues ranging from 2 to 15 amino acids in length. One or more insertions may be introduced into DP-178 (SEQ ID:1), DP-178 fragments, analogs and/or DP-178 homologs (described below).

Deletions of DP-178 (SEQ ID:1), DP-178 fragments, analogs, and/or DP-178 homologs (described below) are also within the scope of the invention. Such deletions consist of the removal of one or more amino acids from the DP-178 or DP-178-like peptide sequence, with the lower limit length of the resulting peptide sequence being 4 to 6 amino acids. Such deletions may involve a single contiguous or greater than one discrete portion of the peptide sequences.

The peptides of the invention may further include homologs of DP-178 (SEQ ID:1) and/or DP-178 truncations which exhibit antiviral activity. Such DP-178 homologs are peptides whose amino acid sequences are comprised of the amino acid sequences of peptide regions of other (i.e., other than HIV-1_{LAI}) viruses that correspond to the gp41 peptide region from which DP-178 (SEQ ID:1) was derived. Such viruses may include, but are not limited to, other HIV-1 isolates and HIV-2 isolates. DP-178 homologs derived from the corresponding gp41 peptide region of other (i.e., non HIV-1_{LAI}) HIV-1 isolates may include, for example, peptide sequences as shown below.

NH_2-YTNTIYTLLEESQNQQEKNEQELLELDKWASLWNWF-COOH (DP-185; SEQ ID:3);

NH_2-YTGIIYNLLEESQNQQEKNEQELLELDKWANLWNWF-COOH (SEQ ID:4);

NH_2-YTSLIYSLLEKSQIQQEKNEQELLELDKWASLWNWF-COOH (SEQ ID:5).

SEQ ID:3 (DP-185), SEQ ID:4, and SEQ ID:5 are derived from HIV-1_{SF2}, HIV-1_{RF}, and HIV-1_{MN} isolates, respectively. Underlined amino acid residues refer to those residues that differ from the corresponding position in the DP-178 (SEQ ID:1) peptide. One such DP-178 homolog, DP-185 (SEQ ID:3), is described in the Working Example presented in Section 6, below, where it is demonstrated that DP-185 (SEQ ID:3) exhibits antiviral activity. The DP-178 homologs of the invention may also include truncations, amino acid substitutions, insertions, and/or deletions, as described above.

In addition, striking similarities, as shown in FIG. 1, exist within the regions of HIV-1 and HIV-2 isolates which correspond to the DP-178 sequence. A DP-178 homolog derived from the HIV-2_{NIHZ} isolate has the 36 amino acid sequence (reading from amino to carboxy terminus):

NH_2-LEANISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-COOH (SEQ ID:7)

Table III and Table IV show some possible truncations of the HIV-2_{NIHZ} DP-178 homolog, which may comprise peptides of between 3 and 36 amino acid residues (i.e., peptides ranging in size from a tripeptide to a 36-mer polypeptide). Peptide sequences in these tables are listed from amino (left) to carboxy (right) terminus. "X" may represent an amino group ($-NH_2$) and "Z" may represent a carboxyl (-COOH) group. Alternatively, as described below, "X" and/or "Z" may represent a hydrophobic group, an acetyl group, a FMOC group, an amido group, or a covalently attached macromolecule, as described below.

TABLE III

HIV-2_{NIHZ} DP-178 homolog carboxy truncations.

X-LEA-Z
X-LEAN-Z
X-LEANI-Z
X-LEANIS-Z
X-LEANISQ-Z
X-LEANISQS-Z
X-LEANISQSL-Z
X-LEANISQSLE-Z
X-LEANISQSLEQ-Z
X-LEANISQSLEQA-Z
X-LEANISQSLEQAQ-Z
X-LEANISQSLEQAQI-Z
X-LEANISQSLEQAQIQ-Z
X-LEANISQSLEQAQIQQ-Z
X-LEANISQSLEQAQIQQE-Z
X-LEANISQSLEQAQIQQEK-Z
X-LEANISQSLEQAQIQQEKN-Z
X-LEANISQSLEQAQIQQEKNM-Z
X-LEANISQSLEQAQIQQEKNMY-Z
X-LEANISQSLEQAQIQQEKNMYE-Z
X-LEANISQSLEQAQIQQEKNMYEL-Z
X-LEANISQSLEQAQIQQEKNMYELQ-Z
X-LEANISQSLEQAQIQQEKNMYELQK-Z
X-LEANISQSLEQAQIQQEKNMYELQKL-Z
X-LEANISQSLEQAQIQQEKNMYELQKLN-Z
X-LEANISQSLEQAQIQQEKNMYELQKLNS-Z
X-LEANISQSLEQAQIQQEKNMYELQKLNSW-Z
X-LEANISQSLEQAQIQQEKNMYELQKLNSWD-Z
X-LEANISQSLEQAQIQQEKNMYELQKLNSWDV-Z
X-LEANISQSLEQAQIQQEKNMYELQKLNSWDVF-Z
X-LEANISQSLEQAQIQQEKNMYELQKLNSWDVFT-Z
X-LEANISQSLEQAQIQQEKNMYELQKLNSWDVFTN-Z
X-LEANISQSLEQAQIQQEKNMYELQKLNSWDVFTNW-Z
X-LEANISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z

The one letter amino acid code is used.

Additionally,

"X" may represent an amino group, a hydrophobic group, including but not limited to carbobenzoxyl, dansyl, or T-butyloxycarbonyl; an acetyl group; a 9-fluorenylmethoxy-carbonyl (FMOC) group; a macromolecular carrier group including but not limited to lipid-fatty acid conjugates, polyethylene glycol, or carbohydrates.

"Z" may represent a carboxyl group; an amido group; a T-butyloxycarbonyl group; a macromolecular carrier group including but not limited to lipid-fatty acid conjugates, polyethylene glycol, or carbohydrates.

TABLE IV

HIV-2_{NIHZ} DP-178 homolog amino truncations.

X-NWL-Z
X-TNWL-Z
X-FTNWL-Z
X-VFTNWL-Z
X-DVFTNWL-Z
X-WDVFTNWL-Z
X-SWDVFTNWL-Z
X-NSWDVFTNWL-Z
X-LNSWDVFTNWL-Z
X-KLNSWDVFTNWL-Z
X-QKLNSWDVFTNWL-Z
X-LQKLNSWDVFTNWL-Z
X-ELQKLNSWDVFTNWL-Z
X-YELQKLNSWDVFTNWL-Z
X-MYELQKLNSWDVFTNWL-Z
X-NMYELQKLNSWDVFTNWL-Z
X-KNMYELQKLNSWDVFTNWL-Z
X-EKNMYELQKLNSWDVFTNWL-Z
X-QEKNMYELQKLNSWDVFTNWL-Z
X-QQEKNMYELQKLNSWDVFTNWL-Z
X-IQQEKNMYELQKLNSWDVFTNWL-Z
X-QIQQEKNMYELQKLNSWDVFTNWL-Z
X-AQIQQEKNMYELQKLNSWDVFTNWL-Z
X-QAQIQQEKNMYELQKLNSWDVFTNWL-Z
X-EQAQIQQEKNMYELQKLNSWDVFTNWL-Z
X-LEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
X-SLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
X-QSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
X-SQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
X-ISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
X-NISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
X-ANISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
X-EANISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
X-LEANISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z

The one letter amino acid code is used.

Additionally,

"X" may represent an amino group, a hydrophobic group, including but not limited to carbobenzoxyl, dansyl, or T-butyloxycarbonyl; an acetyl group; a 9-fluorenylmethoxy-carbonyl (FMOC) group; a macromolecular carrier group including but not limited to lipid-fatty acid conjugates, polyethylene glycol, or carbohydrates.

"Z" may represent a carboxyl group; an amido group; a T-butyloxycarbonyl group; a macromolecular carrier group including but not limited to lipid-fatty acid conjugates, polyethylene glycol, or carbohydrates.

5.2. DP-107 and DP-178 ANALOGOUS ANTIVIRAL PEPTIDES

Peptide sequences functionally corresponding, and thus analogous to, the DP-178 sequences of the invention, described, above, in Section 5.1 may be found in other, non-HIV-1 envelope viruses. Further, peptide sequences functionally corresponding, and thus analogous to, DP-107, an HIV-1-derived antiviral peptide, may also be found in other, non-HIV-1 envelope viruses. DP-107 is a 38 amino acid peptide corresponding to residues 558 to 595 of HIV-1_{LAI} transmembrane (TM) gp41 protein, which exhibits potent anti-viral activity. DP-107 is more fully described in Applicant's co-pending U.S. Patent Application Ser. No. 07/927,532. These DP-107-like and DP-178-like analogous peptides and present in TM proteins of envelope viruses and preferably exhibit antiviral activity, most preferably antiviral activity which is specific to the virus in which their native sequences are found.

DP-107-like and DP-178-like peptides may be identified, for example, by utilizing a computer-assisted search strategy such as that described and demonstrated, below, in the Examples presented in Sections 9 through 16. The search strategy identifies regions in other viruses that are similar in predicted secondary structure to DP-107 and DP-178.

This search strategy is described fully, below, in the Example presented in Section 9. While this search strategy is based, in part, on a primary amino acid motif deduced from DP-107 and DP-178, it is not based solely on searching for primary amino acid sequence homologies, as such protein sequence homologies exist within, but not between major groups of viruses. For example, primary amino acid sequence homology is high within the TM protein of different

strains of HIV-1 or within the TM protein of different isolates of simian immunodeficiency virus (SIV). Primary amino acid sequence homology between HIV-1 and SIV, however, is low enough so as not to be useful. It is not possible, therefore, to find DP-107 or DP-178-like peptides within other viruses, whether structurally, or otherwise, based on primary sequence homology, alone.

Further, while it would be potentially useful to identify primary sequence arrangements of amino acids based on the physical chemical characteristics of different classes of amino acids rather than based on the specific amino acids themselves, for instance, a by concentrating on the coiled-coil nature of the peptide sequence, a computer algorithm designed by Lupas et al. to identify such coiled-coil propensities of regions within proteins (Lupas, A., et al., 1991 Science 252:1162-1164) is inadequate for identifying protein regions analogous to DP-107 or DP-178.

Specifically, analysis of HIV-1 gp160 (containing both gp120 and gp41) using the Lupas algorithm does not identify the coiled-coil region within DP-107. It does, however, identify a region within DP-178 beginning eight amino acids N-terminal to the start of DP-178 and ending eight amino acids from the C-terminus. The DP-107 peptide has been shown experimentally to form a stable coiled coil. A search based on the Lupas search algorithm, therefore, would not have identified the DP-107 coiled-coil region. Conversely, the Lupas algorithm identified the DP-178 region as a potential coiled-coil motif. However, the peptide DP-178 derived from this region failed to form a coiled coil in solution. A possible explanation for the inability of the Lupas search algorithm to accurately identify coiled-coil sequences within the HIV-1 TM, is that the Lupas algorithm is based on the

structure of coiled coils from proteins that are not structurally or functionally similar to the TM proteins of viruses, antiviral peptides (e.g. DP-107 and DP-178) of which are an object of this invention.

The computer search strategy of the invention, as demonstrated in the Examples presented below, in Sections 9 through 16, successfully identifies regions of viral TM proteins similar to DP-107 or DP-178. This search strategy was designed to be used with a commercially-available sequence database packages, preferably PC/Gene. A series of motifs were designed and engineered to range in stringency from very strict to very broad, as discussed in Section 9.

Among the protein sequence seach motifs which may be utilized in such a computer-assisted DP-107-like and DP-178-like antiviral peptide search are the 107x178x4 motif, the ALLMOTI5 motif, and the PLZIP series of motifs, each of which is described in the Example presented in Section 9, below, with 107x178x4 being preferred.

Coiled-coiled sequences are thought to consist of heptad amino acid repeats. For ease of description, the amino acid positions within the heptad repeats are sometimes referred to as A through G, with the first position being A, the second B, etc. The motifs used to identify DP-107-like and DP-178-like sequences herein are desined to specifically search for and identify such heptad repeats. In the descriptions of each of the motifs described, below, amino acids enclosed by brackets , i.e., [], designate the only amino acid residues that are acceptable at the given position, while amino acids enclosed by braces, i.e., {}, designate the only amino acids which are unacceptable at the given heptad position. When a set of bracketed or braced amino acids is followed by a number in parentheses i.e., (), it refers to the

number of subsequent amino acid positions for which the designated set of amino acids hold, e.g, a (2) means "for the next two heptad amino acid positions.

The ALLMOTI5 is written as follows:

{CDGHP]-{CFP}(2)-{CDGHP}-{CFP}(3)-
{CDGHP]-{CFP}(2)-{CDGHP}-{CFP}(3)-
{CDGHP]-{CFP}(2)-{CDGHP}-{CFP}(3)-
{CDGHP]-{CFP}(2)-{CDGHP}-{CFP}(3)-
{CDGHP]-{CFP}(2)-{CDGHP}-{CFP}(3)-

Translating this mofif, it would read: "at the first (A) position of the heptad, any amino acid residue except C, D, G, H, or P is acceptable, at the next two (B,C) amino acid positions, any amino acid residue except C, F, or P is accepatble, at the fourth heptad position (D), any amino acid residue except C, D, G, H, or P is acceptable, at the next three (E, F, G) amino acid positions, any amino acid residue except C, F, or P is acceptable. This motif is designed to search for five consecutive heptad repeats (thus the repeat of the first line five times), meaning that it searches for 35-mer sized peptides. It may also be designed to search for 28-mers, by only repeating the initial motif four times. With respect to the ALLMOTI5 motif, a 35-mer search is preferred. Those viral sequences identified via such an ALLMOTI5 motif are listed in Table V, below, at the end of this Section. The viral sequences listed in Table V potentially exhibit antiviral activity, may be useful in the the identification of antiviral compounds, and are intended to be within the scope of the invention.

The 107x178x4 motif is written as follows:

[EFIKLNQSTVWY]-{CFMP}(2)-[EFIKLNQSTVWY]-{CFMP}(3)-
[EFIKLNQSTVWY]-{CFMP}(2)-[EFIKLNQSTVWY]-{CFMP}(3)-
[EFIKLNQSTVWY]-{CFMP}(2)-[EFIKLNQSTVWY]-{CFMP}(3)-
[EFIKLNQSTVWY]-{CFMP}(2)-[EFIKLNQSTVWY]-{CFMP}(3)-

Translating this mofif, it would read: "at the first (A) position of the heptad, any amino acid residue except E, F, I, K, L, N, Q, S, T, V, W, or Y

is acceptable, at the next two (B,C) amino acid positions, any amino acid residue except C, F, M or P is accepatble, at the fourth position (D), any amino acid residue except E, F, I, K, L, N, Q, S, T, V, W, or Y is acceptable, at the next three (E, F, G) amino acid positions, any amino acid residue except C, F, M or P is acceptable. This motif is designed to search for four consecutive heptad repeats (thus the repeat of the first line four times), meaning that it searches for 28-mer sized peptides. It may also be designed to search for 35-mers, by repeating the initial motif five times. With respect to the 107x178x4 motif, a 28-mer search is preferred. Those viral sequences identified via such a 107x178x4 motif are listed in Table V, below, at the end of this Section. The viral sequences listed in Table V potentially exhibit antiviral activity, may be useful in the the identification of antiviral compounds, and are intended to be within the scope of the invention.

The PLZIP series of motifs are as listed in FIG. 19. These motifs are designed to identify leucine zipper coiled-coil like heptads wherein at least one proline residue is present at some predefined distance N-terminal to the repeat. These PLZIP motifs find regions of proteins with similarities to HIV-1 DP-178 generally located just N-terminal to the transmembrane anchor. These motifs may be translated according to the same convention described above. Each line depicted in FIG. 19 represents a single, complete search motif. "X" in these motifs refers to any amino acid residue. In instances wherein a motif contains two numbers within parentheses, this refers to a variable number of amino acid residues. For example, X (1,12)is translated to "the next one to twelve amino acid residues, inclusive, may be any amino acid".

Tables VI through X, below, at the end of this

Section, list hits from such PLZIP motifs. The viral sequences listed in Table VI through X potentially exhibit antiviral activity, may be useful in the the identification of antiviral compounds, and are intended to be within the scope of the invention.

The Examples presented in Sections 17 and 18, below, demonstrate that respiratory syncytial virus and parainfluenza virus sequences identified via such a computer search exhibit antiviral and/or structural characteristics similar to those of DP-107 or DP-178.

The DP-107-like and DP-178-like analogous peptides may, further, contain any of the additional groups described for DP-178, above, in Section 5.1. For example, these peptides may include any of the additional amino-terminal groups which "X" of Tables I through IV may represent, and may also include any of the carboxy-terminal groups which "Z" of Tables I through IV may represent.

Additionally, such DP-107-like and DP-178-like peptides may furthr include DP-107-like or DP-178-like peptides, such as those listed in Tables V through X, above, containing one or more amino acid substitutions, insertions, and/or deletions. Also, analogs of such DP-107-like and DP-178-like peptides are intended to be within the scope of the invention. Such analogs of the invention may exhibit increased antiviral activity, and may, further, posses increased bioavailability, and/or stability, or reduced immune recognition.

The DP-107-like and DP-178-like amino acid substitutions, insertions and deletions, are as described for DP-178, above, in Section 5.1. Analog modifications are as described, below, in Section 5.3.

TABLE V

Search Results Summary for 107x178x4 and ALLMOTI5 Motifs

107x178x4						ALLMOTI5							
LIBRARY FILE						LIBRARY FILE							
PENV_AVIRE	420-468					PENV1_FRSFV	341-375						
PENV_AVISN	426-474					PENV2_FRSFV	341-378						
PENV_BAEVM	395-452					PENV_AVIRE	420-472						
PENV_BIV08	544-603	631-695				PENV_AVISN	426-478						
PENV_BIV27	573-632	660-724				PENV_BAEVM	390-466						
PENV_BLVAF	304-377					PENV_BIV08	530-610	635-695					
PENV_BLVAU	304-377					PENV_BIV27	559-639	664-724					
PENV_BLVAV	304-377					PENV_BLVAF	304-379						
PENV_BLVB2	311-377					PENV_BLVAU	304-379						
PENV_BLVB5	304-377					PENV_BLVAV	304-379						
PENV_BLVJ	304-377					PENV_BLVB2	304-379						
PENV_CAEVG	165-192					PENV_BLVB5	304-379						
PENV_EIAV1	668-712					PENV_BLVJ	304-379						
PENV_EIAV2	668-695					PENV_CAEVC	157-196	615-720	761-785	847-895			
PENV_EIAV3	668-712					PENV_CAEVG	154-193	613-718	749-783	845-893			
PENV_EIAV5	668-696					PENV_EIAV1	436-525	559-593	668-716				
PENV_EIAV8	668-712					PENV_EIAV2	436-525	559-593	658-692				
PENV_EIAVC	668-712					PENV_EIAV3	436-525	559-593	658-716				
PENV_EIAVW	668-712					PENV_EIAV5	437-526	560-594	659-693				
PENV_EIAVY	668-712					PENV_EIAV8	436-525	559-593	658-716				
PENV_FENV1	517-544					PENV_EIAVC	436-525	559-593	658-716				
PENV_FIVPE	650-680	722-749.				PENV_EIAVW	436-525	559-593	658-716				
PENV_FIVSD	639-668	720-747				PENV_EIAVY	436-525	559-593	658-716				
PENV_FIVT2	640-679	721-748				PENV_FENV1	503-555	587-604					
PENV_FLVC8	509-538					PENV_FIVPE	610-690	715-756					
PENV_FLVGL	490-519					PENV_FIV8D	601-688	713-754					
PENV_FLVLB	510-539					PENV_FIVT2	609-689	714-755					
PENV_FLVSA	487-516					PENV_FLVC8	497-549	561-595					
PENV_FOAMV	318-355	866-893				PENV_FLVGL	478-530	542-576					
PENV_FSVGA	510-539					PENV_FLVLB	498-550	562-596					
PENV_FSVGB	490-519					PENV_FLVSA	475-527	539-573					
PENV_FSVSM	493-522					PENV_FOAMV	321-355	563-693	886-903				
PENV_GALV	523-564					PENV_FRSFB	318-354						
PENV_HTL1A	342-376					PENV_FSVGA	498-550	562-596					
PENV_HTL1C	342-376					PENV_FSVGB	478-530	542-576					
PENV_HTL1M	342-376					PENV_FSVSM	481-524	545-579					
PENV_HTLV2	338-370					PENV_FSVST	498-532						
PENV_HV1A2	544-592	630-682	780-825			PENV_GALV	523-575	587-621					
PENV_HV1B1	545-594	631-683	791-818			PENV_HTL1A	321-363						
PENV_HV1B8	540-589	628-678	786-813			PENV_HTL1C	316-363						
PENV_HV1BN	562-590	628-679	787-815			PENV_HTL1M	321-363						
PENV_HV1BR	550-599	638-688	796-823			PENV_HTLV2	317-377						
PENV_HV1C4	557-606	643-695	803-835			PENV_HV1A2	497-593	612-711	766-845				
PENV_HV1EL	543-591	628-680				PENV_HV1B1	505-594	610-712	767-843				
PENV_HV1H2	545-594	631-683	791-818			PENV_HV1B8	500-589	605-707	762-838				

PENV_HV1H3	545-594	631-683	791-818			PENV_HV1BN	601-590	609-708	763-831				
PENV_HV1J3	556-605	642-694	802-829			PENV_HV1BR	610-599	616-717	772-841				
PENV_HV1JR		622-675	783-811			PENV_HV1C4	610-606	628-724	779-855				
PENV_HV1KB	555-596	637-677	776-824			PENV_HV1EL	602-591	607-709	766-829				
PENV_HV1MA	547-595	633-707	794-826			PENV_HV1H2	505-594	610-712	767-836				
PENV_HV1MF	543-592	629-681	788-816			PENV_HV1H3	505-594	610-712	767-843				
PENV_HV1MN	567-595	632-684	791-819			PENV_HV1J3	517-605	622-723	778-843				
PENV_HV1ND	536-583	621-673	783-813			PENV_HV1JR	497-586	603-704	759-835				
PENV_HV1OY	544-593	630-704	789-820			PENV_HV1KB	511-545	555-599	818-718	772-848			
PENV_HV1PV	545-594	631-683	791-818			PENV_HV1MA	507-596	617-714	770-825				
PENV_HV1RH	554-602	640-692	800-832			PENV_HV1MF	503-592	622-710	765-841				
PENV_HV1S1	536-585	622-674	782-809			PENV_HV1MN	506-595	617-713	774-841				
PENV_HV1S3	541-589	627-679	787-815			PENV_HV1ND	495-584	601-702	757-825				
PENV_HV1SC	545-593	631-683				PENV_HV1OY	497-593	610-711	766-842				
PENV_HV1W1	545-593	631-683	791-818			PENV_HV1PV	505-594	610-712	767-843				
PENV_HV1W2	536-584	622-674	782-809			PENV_HV1RH	507-603	618-721	776-852				
PENV_HV1Z2	542-591	628-680	790-820			PENV_HV1S1	496-585	602-703	758-830				
PENV_HV1Z6	545-593	630-682	792-822			PENV_HV1S3	494-590	607-708	763-837				
PENV_HV1Z8	573-601	634-678	797-828			PENV_HV1SC	498-594	611-712	767-834				
PENV_HV1ZH	545-594	627-666	791-823			PENV_HV1W1	498-594	611-712	767-836				
PENV_HV2BE	532-591	621-648	653-697			PENV_HV1W2	489-584	602-703	758-827				
PENV_HV2CA	534-593	623-650	655-699			PENV_HV1Z2	502-591	607-709	764-831				
PENV_HV2D1	523-550	555-582	644-688			PENV_HV1Z6	504-593	609-711	766-840				
PENV_HV2G1	524-551	556-583	613-640	645-693		PENV_HV1Z8	512-601	617-675	682-719	774-831			
PENV_HV2NZ	524-551	556-583	613-640	692-689		PENV_HV1ZH	522-594	612-712	777-839				
PENV_HV2RO	533-592	622-698				PENV_HV2BE	510-595	617-680					
PENV_HV2S2	527-554	559-586	648-682			PENV_HV2CA	512-597	619-709					
PENV_HV2SB	557-584	614-673				PENV_HV2D1	501-586	608-698					
PENV_HV2ST	527-554	559-586	648-692			PENV_HV2G1	502-587	609-699					
PENV_MCFF	473-512					PENV_HV2NZ	488-587	609-699					
PENV_MCFF3	488-516					PENV_HV2RO	511-598	618-708					
PENV_MLVAV	517-544					PENV_HV2S2	505-590	612-702					
PENV_MLVCB	510-539					PENV_HV2SB	526-588	614-700					
PENV_MLVF5	523-553					PENV_HV2ST	505-590	612-702					
PENV_MLVFF	523-553					PENV_IPMAE	387-422	465-527					
PENV_MLVFP	523-553					PENV_JSRV	403-455	571-605					
PENV_MLVHO	510-540					PENV_MCFF	473-525	537-571					
PENV_MLVKI	40-81					PENV_MCFF3	474-526	538-572					
PENV_MLVMO	502-543					PENV_MLVAV	503-555	567-601					
PENV_MLVRD	497-538					PENV_MLVCB	498-550	562-596					
PENV_MLVRK	497-538					PENV_MLVF5	520-564	576-610					
PENV_MMTV8	456-485	562-589				PENV_MLVFF	520-564	576-610					
PENV_MMTVG	456-485	562-589				PENV_MLVFP	520-564	576-610					
PENV_MPMV	422-470					PENV_MLVHO	504-551	563-597					
PENV_M9VFB	57-84					PENV_MLVKI	40-92	104-138					
PENV_OMVV8	42-69	196-223	780-807			PENV_MLVMO	502-554	566-600					
PENV_RMCFV	487-517					PENV_MLVRD	497-549	561-595					

PENV_SFV1	14-41	866-901				PENV_MLVRK	497-549	561-595					
PENV_SFV3L	18-45	319-357	673-700	883-898		PENV_MMTVB	477-539	556-612					
PENV_SIVA1	561-588	592-619	652-679	697-724		PENV_MMTVG	477-539	556-612					
PENV_SIVAG	566-593	597-624	658-685	703-730		PENV_MPMV	408-474						
PENV_SIVAI	548-603	634-706				PENV_MSVFB	43-95	107-141					
PENV_SIVAT	590-617	651-678				PENV_OMVV6	22-64	185-223	664-746	780-818			
PENV_SIVCZ	528-584	627-654				PENV_RMCFV	484-528	540-574					
PENV_SIVGB	588-650	784-816				PENV_RSFFV	342-376						
PENV_SIVM1	550-609	671-715				PENV_SFV1	1-41	101-140	154-205	321-355	563-651	858-893	868-904
PENV_SIVM2	156-215	277-289				PENV_SFV3L	5-46	158-209	319-357	580-706	883-901		
PENV_SIVMK	563-608					PENV_SIVA1	289-310	551-623	643-693				
PENV_SIVML	549-608					PENV_SIVAG	556-628	651-699	808-852				
PENV_SIV84	563-612	642-668	691-718			PENV_SIVAI	257-291	336-370	535-607	627-684	782-840		
PENV_SIVSP	554-595	646-722				PENV_SIVAT	284-288	549-621	644-692	798-833			
PENV_SMRVH	400-462					PENV_SIVCZ	253-291	330-365	512-584	669-703	803-837		
PENV_SRV1	408-471					PENV_SIVGB	566-654	677-725					
PENV_VILV	773-800					PENV_SIVM1	114-151	465-506	528-613	635-725	809-864		
PENV_VILV1	780-807					PENV_SIVM2	71-116	134-219	245-331				
PENV_VILV2	782-809					PENV_SIVMK	464-505	540-612	638-724				
PHEMA_CVBLY	208-242					PENV_SIVML	464-505	540-612	638-724				
PHEMA_CVBM	208-242					PENV_SIV84	466-509	517-616	638-728	812-853			
PHEMA_CVBQ	208-242					PENV_SIVSP	470-513	521-620	642-732	811-848			
PHEMA_CVHOC	208-242					PENV_SMRVH	400-466						
PHEMA_IAAIC	387-453					PENV_SRV1	408-476						
PHEMA_IABAN	371-437					PENV_VILV	21-62	184-222	637-740	773-809			
PHEMA_IABUD	381-451					PENV_VILV1	21-62	184-222	643-746	780-816			
PHEMA_IACKA	381-451					PENV_VILV2	21-62	184-222	645-748	782-818			
PHEMA_IACKG	382-441	494-528				PHEMA_CVBLY	208-242						
PHEMA_IACKP	396-426					PHEMA_CVBM	208-242						
PHEMA_IACKQ	396-426					PHEMA_CVBQ	208-242						
PHEMA_IACKV	384-443					PHEMA_CVHOC	208-242						
PHEMA_IADA1	381-451					PHEMA_IAAIC	380-456						
PHEMA_IADA2	423-453	499-543				PHEMA_IABAN	364-440						
PHEMA_IADA3	387-453					PHEMA_IABUD	378-454						
PHEMA_IADA4	418-478					PHEMA_IACKA	378-454						
PHEMA_IADCZ	381-451					PHEMA_IACKG	108-142	375-475	494-528				
PHEMA_IADE1	402-453	506-533				PHEMA_IACKP	380-452	487-532					
PHEMA_IADH1	371-437					PHEMA_IACKQ	380-452	487-532					
PHEMA_IADH2	371-437					PHEMA_IACKS	377-469	504-549					
PHEMA_IADH3	371-437					PHEMA_IACKV	112-146	377-469					
PHEMA_IADH4	371-437					PHEMA_IADA1	377-454						
PHEMA_IADH5	371-437					PHEMA_IADA2	377-478	495-547					
PHEMA_IADH6	371-437					PHEMA_IADA3	380-453						
PHEMA_IADH7	371-437					PHEMA_IADA4	378-478	508-548					
PHEMA_IADIR	415-445					PHEMA_IADCZ	378-454						
PHEMA_IADM2	387-453					PHEMA_IADE1	21-55	377-472					
PHEMA_IADNZ	381-451					PHEMA_IADH1	364-440						

PHEMA_IADU3	387-453					PHEMA_IADH2	384-440						
PHEMA_IAEN7	387-453					PHEMA_IADH3	384-440						
PHEMA_IAFPR	384-442					PHEMA_IADH4	384-440						
PHEMA_IAGRE	381-451					PHEMA_IADH5	384-440						
PHEMA_IAGU2	505-532					PHEMA_IADH6	384-440						
PHEMA_IAGUA	504-531					PHEMA_IADH7	384-440						
PHEMA_IAHAL	386-452					PHEMA_IADIR	376-471	506-551					
PHEMA_IAHC6	388-457					PHEMA_IADM1	21-55						
PHEMA_IAHC7	388-457					PHEMA_IADM2	380-456						
PHEMA_IAHCD	388-457					PHEMA_IADNY	21-55						
PHEMA_IAHDE	388-457					PHEMA_IADNZ	376-454						
PHEMA_IAHFO	386-452					PHEMA_IADU1	21-55						
PHEMA_IAHK6	386-452					PHEMA_IADU3	380-456						
PHEMA_IAHK7	386-452					PHEMA_IAEN7	380-456						
PHEMA_IAHLE	388-457					PHEMA_IAFPR	377-477						
PHEMA_IAHLO	388-457					PHEMA_IAGRE	376-454						
PHEMA_IAHMI	388-452					PHEMA_IAGU2	376-473						
PHEMA_IAHNM	386-452					PHEMA_IAGUA	377-476						
PHEMA_IAHNN	388-457					PHEMA_IAHAL	379-455						
PHEMA_IAHPR	388-457					PHEMA_IAHC6	112-146	380-484	503-537				
PHEMA_IAHRO	386-452					PHEMA_IAHC7	112-146	380-484	503-537				
PHEMA_IAHSA	386-452					PHEMA_IAHCD	380-484	503-537					
PHEMA_IAHSP	388-457					PHEMA_IAHDE	380-484	503-537					
PHEMA_IAHSW	388-457					PHEMA_IAHFO	379-455						
PHEMA_IAHTE	386-452					PHEMA_IAHK6	379-455						
PHEMA_IAHTO	386-455					PHEMA_IAHK7	379-455						
PHEMA_IAHUR	386-452					PHEMA_IAHLE	112-146	380-484	503-537				
PHEMA_IAKIE	425-478					PHEMA_IAHLO	112-146	380-484	503-537				
PHEMA_IALEN	425-478					PHEMA_IAHMI	379-455						
PHEMA_IAMAA	380-450					PHEMA_IAHNM	379-455						
PHEMA_IAMAB	385-455					PHEMA_IAHNN	112-146	380-484	503-537				
PHEMA_IAMAO	387-453					PHEMA_IAHPR	112-146	380-484	503-537				
PHEMA_IAME1	387-453					PHEMA_IAHRO	379-455						
PHEMA_IAME2	387-453					PHEMA_IAHSA	379-455						
PHEMA_IAME6	371-437					PHEMA_IAHSP	112-146	380-484	503-537				
PHEMA_IAMIN	382-441					PHEMA_IAHSW	112-146	380-484	503-537				
PHEMA_IANT6	387-453					PHEMA_IAHTE	379-455						
PHEMA_IAPIL	505-534					PHEMA_IAHTO	379-455						
PHEMA_IAPUE	425-478					PHEMA_IAHUR	379-455						
PHEMA_IARUD	381-451					PHEMA_IAJAP	375-467	502-547					
PHEMA_IASE2	381-451					PHEMA_IAKIE	376-478	506-541					
PHEMA_IASH2	506-547					PHEMA_IALEN	376-478	506-548					
PHEMA_IASTA	384-443					PHEMA_IAMAA	377-453						
PHEMA_IATKI	416-445					PHEMA_IAMAB	382-458						
PHEMA_IATKM	381-451					PHEMA_IAMAO	380-456						
PHEMA_IATKO	507-534					PHEMA_IAME1	380-456						
PHEMA_IATKP	424-454	493-539				PHEMA_IAME2	380-456						

PHEMA_IATKR	381-422					PHEMA_IAME6	384-440						
PHEMA_IATKW	419-449	500-536				PHEMA_IAMIN	108-142	375-475					
PHEMA_IAUDO	387-453					PHEMA_IANT6	380-456						
PHEMA_IAUS6	425-478					PHEMA_IAPIL	378-477	496-534					
PHEMA_IAVI7	386-454					PHEMA_IAPUE	376-478	506-548					
PHEMA_IAWIL	424-477					PHEMA_IARUD	378-454						
PHEMA_IAZCO	387-453					PHEMA_IASE2	378-454						
PHEMA_IAZH2	371-437					PHEMA_IASH2	379-474	506-552					
PHEMA_IAZH3	371-437					PHEMA_IASTA	112-146	377-469					
PHEMA_IAZIN	418-478	506-547				PHEMA_IATKI	379-471	506-551					
PHEMA_IAZNJ	418-478	506-547				PHEMA_IATKM	378-454						
PHEMA_IAZUK	387-453					PHEMA_IATKO	392-470	504-548					
PHEMA_INBBE	400-431	439-483				PHEMA_IATKP	378-454	493-540					
PHEMA_INBBO	390-421	429-473				PHEMA_IATKR	30-64	374-474					
PHEMA_INBEN	398-429	437-481				PHEMA_IATKW	373-472	487-539					
PHEMA_INBHK	391-418	429-473				PHEMA_IATRA	21-55						
PHEMA_INBLE	398-430	438-482				PHEMA_IAUDO	387-456						
PHEMA_INBMD	389-420	428-472				PHEMA_IAUS6	376-478	506-548					
PHEMA_INBME	393-424	432-476				PHEMA_IAVI7	381-457						
PHEMA_INBOR	398-429	437-481				PHEMA_IAWIL	375-477	505-547					
PHEMA_INBSI	398-429	437-481				PHEMA_IAZCO	380-456						
PHEMA_INBUS	391-422	430-474				PHEMA_IAZH2	384-440						
PHEMA_INBVI	393-424	432-476				PHEMA_IAZH3	384-440						
PHEMA_INBVK	400-431	439-483				PHEMA_IAZIN	378-478	506-548					
PHEMA_INCCA	495-571					PHEMA_IAZNJ	379-478	506-548					
PHEMA_INCEN	483-559					PHEMA_IAZUK	380-456						
PHEMA_INCGL	483-559					PHEMA_INBBE	388-473						
PHEMA_INCHY	482-558					PHEMA_INBBO	378-463						
PHEMA_INCJH	496-572					PHEMA_INBEN	386-471						
PHEMA_INCKY	482-558					PHEMA_INBHK	381-463						
PHEMA_INCMI	482-558					PHEMA_INBLE	387-472						
PHEMA_INCNA	482-558					PHEMA_INBMD	377-462						
PHEMA_INCP1	483-559					PHEMA_INBME	381-468						
PHEMA_INCP2	483-559					PHEMA_INBOR	386-471						
PHEMA_INCP3	483-559					PHEMA_INBSI	386-471						
PHEMA_INCTA	483-559					PHEMA_INBUS	379-464						
PHEMA_INCYA	483-559					PHEMA_INBVI	381-466						
PHEMA_NDVA	64-91					PHEMA_INBVK	388-473						
PHEMA_NDVB	64-91					PHEMA_INCCA	483-571						
PHEMA_NDVD	64-91					PHEMA_INCEN	471-559						
PHEMA_NDVH	64-91					PHEMA_INCGL	471-559						
PHEMA_NDVI	64-91					PHEMA_INCHY	470-558						
PHEMA_NDVM	64-91					PHEMA_INCJH	484-572						
PHEMA_NDVQ	64-91					PHEMA_INCKY	470-558						
PHEMA_NDVTG	64-91					PHEMA_INCMI	470-558						
PHEMA_NDVU	64-91					PHEMA_INCNA	470-558						
PHEMA_PHODV	39-66	46-73				PHEMA_INCP1	471-559						

PHEMA_PI1HW	79-110	366-393				PHEMA_INCP2	471-559						
PHEMA_PI3B	66-93					PHEMA_INCP3	471-559						
PHEMA_PI3H4	27-61					PHEMA_INCTA	471-559						
PHEMA_PI3HA	27-61					PHEMA_INCYA	471-559						
PHEMA_PI3HT	27-76					PHEMA_MEASE	46-90						
PHEMA_PI3HU	23-70					PHEMA_MEASH	46-90						
PHEMA_PI3HV	27-61					PHEMA_MEASI	46-87						
PHEMA_PI3HW	27-61					PHEMA_MEASY	46-87						
PHEMA_PI3HX	27-61					PHEMA_MUMPM	34-99						
PHEMA_RACVI	166-214	256-283				PHEMA_MUMPR	34-99						
PHEMA_SEND5	79-106					PHEMA_MUMPS	34-99						
PHEMA_SENDF	79-106					PHEMA_NDVA	8-52	477-528					
PHEMA_SENDH	79-106					PHEMA_NDVB	1-49						
PHEMA_SENDJ	79-106					PHEMA_NDVD	1-49						
PHEMA_SENDZ	79-106					PHEMA_NDVM	1-49						
PHEMA_SV41	22-52	394-421				PHEMA_NDVQ	1-49						
PHEMA_VACCC	119-146	175-202	216-243			PHEMA_NDVTG	1-49						
PHEMA_VACCI	109-146	175-202	216-243			PHEMA_NDVU	1-49						
PHEMA_VACCT	119-146	175-202	216-243			PHEMA_PHODV	39-73						
PHEMA_VACCV	109-146	175-202	215-242			PHEMA_PI1HW	66-110						
PVENV_DHVI1	318-366					PHEMA_PI2H	247-281						
PVENV_EAV	120-147					PHEMA_PI2HT	247-281						
PVENV_THOGV	313-347					PHEMA_PI3B	38-93						
PVF03_VACCC	71-110	185-212				PHEMA_PI3H4	13-110	394-428					
PVF03_VACCV	71-110	185-212				PHEMA_PI3HA	20-110	394-428					
PVF05_VACCP	33-60					PHEMA_PI3HT	13-110	394-428					
PVF05_VACCV	33-60					PHEMA_PI3HU	13-110	394-428					
PVF11_VACCC	274-321					PHEMA_PI3HV	13-110	394-428					
PVF11_VACCP	270-317					PHEMA_PI3HW	13-110	394-428					
PVF12_VACCC	10-37	113-140	554-581			PHEMA_PI3HX	13-110	394-428					
PVF12_VACCP	10-37	113-140	554-581			PHEMA_PI4HA	54-88						
PVF16_VACCC	35-62	152-179				PHEMA_RACVI	166-214	256-280					
PVF16_VACCP	35-62	152-179				PHEMA_RINDK	46-87						
PVFP4_FOWPV	146-173					PHEMA_RINDL	46-87	191-225					
PVFU9_ORFNZ	59-86					PHEMA_SEND5	57-110						
PVFU8_VACCC	37-64					PHEMA_SENDF	57-110						
PVFU9_VACCV	37-64					PHEMA_SENDH	57-110						
PVG01_VACCC	226-252	301-335				PHEMA_SENDJ	57-110						
PVG01_VACCV	164-191	240-274				PHEMA_SENDZ	57-110						
PVG01_VARV	226-252	301-335				PHEMA_SV41	18-52	387-421					
PVG02_VACCV	96-123					PHEMA_SV5	27-82						
PVG02_VARV	96-123					PHEMA_SV5LN	27-82						
PVG03_H3VEB	146-176					PVENV_BEV	196-229						
PVG03_H3VEK	146-176					PVENV_DHVI1	318-366						
PVG05_VACCC	48-75	131-161	225-289	355-389		PVENV_MCV1	252-286						
PVG05_VARV	48-75	124-161	255-289	355-389		PVENV_MCV2	252-286						
PVG07_H3VI1	71-98					PVENV_THOGV	313-354						

PVG09_VACCC	308-338					PVENV_VACCC	257-295						
PVG09_VACCV	271-301					PVENV_VACCI	257-295						
PVG09_VARV	308-338					PVENV_VACCP	257-295						
PVG12_SPV1R	11-45					PVENV_VACCV	257-295						
PVG17_HSVI1	177-204					PVF01_VACCC	46-80	124-158					
PVG18_HSVI1	174-208					PVF01_VACCV	46-80	124-158					
PVG1_SPV1R	260-287					PVF03_VACCC	71-110						
PVG1_SPV4	287-314	383-410				PVF03_VACCV	71-110						
PVG22_HSVI1	373-400	581-622	668-705	766-824		PVF05_VACCC	81-129	282-320					
PVG24_HSVI1	31-58					PVF05_VACCP	81-129	282-320					
PVG28_HSVI1	253-290	497-528				PVF05_VACCV	81-129	283-321					
PVG2R_AMEPV	33-64	91-118				PVF11_VACCC	217-258	269-316					
PVG2_SPV1R	286-326					PVF11_VACCP	213-254	265-311					
PVG2_SPV4	146-173	175-205	262-310			PVF12_VACCC	1-67	102-143	199-236	350-388	544-581		
PVG34_HSVI1	95-122					PVF12_VACCP	1-67	102-143	199-236	350-388	644-681		
PVG37_HSVI1	442-469					PVF16_VACCC	155-194						
PVG39_HSVI1	651-678	1086-1115				PVF16_VACCP	155-194						
PVG3L_AMEPV	2-29					PVFP3_FOWPV	1-43						
PVG3_SPV1R	15-49					PVFP4_FOWPV	139-173	239-273					
PVG3_SPV4	18-52	87-148				PVFP7_FOWPV	23-57						
PVG45_HSVSA	138-165					PVFPL_FOWP1	77-111						
PVG46_HSVI1	142-169	348-373	897-924	973-1007		PVFUS_VACCC	30-64						
PVG48_HSVSA	380-394					PVFUS_VACCV	30-64						
PVG4R_AMEPV	4-31					PVG01_BPP22	94-135	400-468	475-513	608-659			
PVG4_SPV1R	116-146					PVG01_HSVI1	271-306	512-563	591-647	730-764			
PVG51_HSVI1	34-61	87-114				PVG01_VACCC	301-339						
PVG52_HSVSA	47-74					PVG01_VACCV	240-278						
PVG56_HSVI1	582-609					PVG01_VARV	301-339						
PVG5_SPV1R	66-92					PVG03_HSVEB	143-177						
PVG5_SPV4	56-83					PVG03_HSVEK	143-177						
PVG63_HSVI1	550-584					PVG03_VARV	64-98						
PVG64_HSVI1	477-504					PVG05_VACCC	117-158	255-289	355-389				
PVG65_HSVI1	1213-1254					PVG05_VARV	117-158	255-289	355-389				
PVG66_HSVI1	382-408					PVG06_HSVI1	61-109						
PVG67_HSVI1	1342-1389					PVG07_HSVI1	69-103						
PVG68_HSVI1	261-288					PVG07_VACCC	114-175	324-358					
PVG72_HSVI1	447-481					PVG07_VARV	114-175	324-358					
PVG75_HSVI1	388-422					PVG09_VACCC	304-338						
PVG76_HSVI1	200-227					PVG09_VACCV	267-301						
PVG7_SPV4	14-44					PVG09_VARV	304-338						
PVGF1_IBVB	1230-1260	2408-2435				PVG10_HSVI1	63-97						
PVGL2_CVBF	399-426	642-676	1022-1084	1278-1305		PVG12_SPV1R	11-45						
PVGL2_CVBL9	399-426		1022-1084	1278-1305		PVG16_HSVSA	58-86						
PVGL2_CVBLY	399-426	642-676	1022-1084	1278-1305		PVG17_HSVI1	92-129	177-211					
PVGL2_CVBM	399-426	642-676	1022-1084	1278-1305		PVG18_HSVI1	174-208	215-256					
PVGL2_CVBQ	399-426	642-676	1022-1084	1278-1305		PVG1L_AMEPV	407-441						
PVGL2_CVBV	399-426	642-676	1022-1084	1278-1305		PVG1_SPV1R	136-170	256-297	320-357				

PVGL2_CVH22	770-797	809-875	1056-1112			PVG1_SPV4	287-321						
PVGL2_CVM4	643-684	1030-1092				PVG22_HSVI1	117-158	437-629	660-692	899-1055			
PVGL2_CVMA5	36-63	591-632	978-1040			PVG24_HSVI1	7-72	74-108					
PVGL2_CVMJH	502-543	889-951				PVG27_HSVI1	164-219						
PVGL2_CVPFS	69-110	692-733	1072-1145	1353-1389		PVG28_HSVI1	253-290						
PVGL2_CVPPU	69-107	690-731	1067-1143	1351-1387		PVG2R_AMEPV	29-63	184-218					
PVGL2_CVPR8	468-509	845-921	1128-1165			PVG2_SPV1R	222-256	285-328					
PVGL2_CVPRM	468-509	845-921	1129-1165			PVG2_SPV4	256-310						
PVGL2_EBV	68-102					PVG33_HSVI1	149-183						
PVGL2_FIPV	189-233	454-481	709-736	1072-1148	1356-1382	PVG34_HSVI1	345-379						
PVGL2_IBV8	809-836	876-903	1057-1091			PVG35_HSVI1	17-90						
PVGL2_IBVB	808-835	875-902	1056-1090			PVG37_HSVI1	435-472						
PVGL2_IBVD2	809-836	876-903	1057-1091			PVG38_HSVI1	84-118						
PVGL2_IBVK	808-835	875-902	1056-1090			PVG39_HSVI1	124-158	266-300					
PVGL2_IBVM	808-835	875-902	1056-1090			PVG3_SPV1R	8-49	162-196	203-244				
PVGLB_EBV	95-122	631-658				PVG3_SPV4	6-54	87-121					
PVGLB_HCMVA	25-88	397-424	440-467	851-878		PVG43_HSVI1	116-150	262-296	324-361	643-677			
PVGLB_HCMVT	50-88	397-424	435-462	852-879		PVG45_HSV6A	121-162						
PVGLB_HSVB1	427-454					PVG46_HSVI1	46-86	939-1078	1251-1321				
PVGLB_HSVB2	447-474					PVG48_HSVI1	169-207						
PVGLB_HSVBC	426-453					PVG48_HSV8A	360-417	611-666	733-767				
PVGLB_HSVE1	443-470	934-961				PVG49_HSV5A	66-102						
PVGLB_HSVE4	486-513	816-843				PVG4R_AMEPV	4-38						
PVGLB_HSVEA	443-470	934-961				PVG4_SPV4	88-130						
PVGLB_HSVEB	443-470	934-961				PVG51_HSVI1	34-73	89-123					
PVGLB_HSVEL	443-470	933-960				PVG51_HSV6A	29-70	123-157	162-196				
PVGLB_HSVMD	93-120	352-379				PVG53_HSVI1	87-127						
PVGLB_MCMV6	381-408	441-475				PVG54_HSVI1	355-396						
PVGLC_HSV11	469-510					PVG55_HSVI1	101-135						
PVGLC_HSV1K	469-510					PVG55_HSV6A	128-178						
PVGLC_HSVEB	124-161					PVG58_HSVI1	151-192	578-612	644-678	750-784	848-880	1111-1145	
PVGLC_HSVMB	63-97					PVG59_HSVI1	10-72	89-123					
PVGLC_HSVMG	62-96					PVG59_HSV8A	169-209						
PVGLC_HSVMM	63-97					PVG5_SPV1R	65-103						
PVGLC_VZVD	295-322					PVG61_HSVI1	265-299						
PVGLC_VZVB	295-322					PVG63_HSVI1	546-584						
PVGLE_HSV2	111-148					PVG65_HSVI1	805-839	1213-1254					
PVGLF_BRSVA	38-65	154-202	216-243	442-469	486-531	PVG66_HSVI1	154-188	328-410					
PVGLF_BRSVC	38-65	154-202	216-243	444-471	488-533	PVG67_HSVI1	379-413	601-546	1321-1369	1478-1541			
PVGLF_BRSVR	38-65	154-202	216-243	444-471	488-533	PVG68_HSVI1	245-288						
PVGLF_CDVO	252-293	340-367				PVG72_HSVI1	447-484	723-757	912-949				
PVGLF_HRSV1	38-65	154-203	442-471	488-515		PVG75_HSVI1	271-305	388-422					
PVGLF_HRSVA	38-65	154-202	213-243	488-518		PVG8_SPV1R	5-51						
PVGLF_HRSVL	38-65	154-202	216-243	444-471	488-515	PVGF1_IBVB	142-178	1233-1267	2119-2156	3388-3424	3475-3513	3517-3556	3761-3795
PVGLF_HRSVR	38-65	154-202	213-243	442-471	488-518	PVGH3_HCMVA	10-44						
PVGLF_MEASE	228-262					PVGL2_CVBF	642-678	850-886	993-1088	1263-1305			
PVGLF_MEASI	231-265		---			PVGL2_CVBL9	850-886	993-1109	1263-1305				

PVGLF_MEA8Y	228-262					PVGL2_CVBLY	642-676	850-885	993-1109	1263-1305			
PVGLF_MUMPM	20-54	447-486				PVGL2_CVBM	642-676	850-885	993-1109	1263-1305			
PVGLF_MUMPR	20-54	447-486				PVGL2_CVBQ	642-676	850-885	993-1109	1263-1305			
PVGLF_MUMPS	151-178	426-511				PVGL2_CVBV	642-676	850-885	993-1109	1263-1305			
PVGLF_NDVA	151-178	426-512				PVGL2_CVH22	770-816	1055-1112					
PVGLF_NDVB	151-178	426-512				PVGL2_CVM4	643-684	1001-1117	1270-1315				
PVGLF_NDVI	151-178	426-512				PVGL2_CVMA5	591-632	949-1079	1218-1263				
PVGLF_NDVM	151-178	426-512				PVGL2_CVMJH	502-543	860-876	1128-1174				
PVGLF_NDVT	151-178	426-512				PVGL2_CVPF9	69-110	446-482	692-733	889-923	1040-1186	1352-1389	
PVGLF_NDVTG	151-178	426-512				PVGL2_CVPPU	69-110	446-480	690-731	887-921	1038-1184	1351-1387	
PVGLF_NDVU	151-178	426-512				PVGL2_CVPR8	224-258	468-509	665-699	816-862	1128-1165		
PVGLF_PHODV	36-63	221-262	309-336			PVGL2_CVPRM	224-258	468-509	665-699	816-862	1128-1165		
PVGLF_PI1HC	147-174	210-266				PVGL2_EBV	68-102						
PVGLF_PI2H	90-117	141-175	238-266	483-528		PVGL2_FIPV	189-245	451-485	695-736	892-926	1043-1189	1355-1392	
PVGLF_PI2HG	90-117	141-175	238-266	483-528		PVGL2_IBV8	791-905	1057-1091					
PVGLF_PI2HT	90-117	141-175	238-266	483-528		PVGL2_IBVB	437-478	772-904	1056-1090				
PVGLF_PI3B	115-182	207-241	459-497			PVGL2_IBVD2	773-905	1057-1091					
PVGLF_PI3H4	115-182	207-241	457-497			PVGL2_IBVK	437-478	772-904	1056-1090				
PVGLF_RINDK	224-265	458-495				PVGL2_IBVM	437-478	772-904	1056-1090				
PVGLF_RINDL	224-265	458-506				PVGLB_HCMVA	43-88	128-162	436-484	844-878			
PVGLF_SEND5	122-149	211-245	480-507			PVGLB_HCMVT	22-88	128-162	437-485	845-879			
PVGLF_SENDF	122-149	211-245	480-507			PVGLB_HSV11	826-880						
PVGLF_SENDH	122-149	211-245	480-507			PVGLB_HSV1F	827-889						
PVGLF_SENDJ	122-149	211-245	480-507			PVGLB_HSV1K	827-889						
PVGLF_SENDZ	122-149	211-245	480-507			PVGLB_HSV1P	826-880						
PVGLF_SV41	144-185	241-269	459-496			PVGLB_HSV23	826-880						
PVGLF_SV5	137-171	417-444				PVGLB_HSV2H	826-880						
PVGLF_TRTV	124-161	193-200	457-484			PVGLB_HSV26	817-871						
PVGLG_BEFV	523-557					PVGLB_HSV6U	37-71	185-223					
PVGLG_BRSVC	92-123					PVGLB_HSVB1	859-913						
PVGLG_HRSV1	63-93					PVGLB_HSVB2	440-474	848-902					
PVGLG_HRSV4	66-107					PVGLB_HSVBC	883-900						
PVGLG_HRSV5	243-273					PVGLB_HSVE1	542-576	911-961					
PVGLG_HRSV8	66-93					PVGLB_HSVE4	474-515	847-900					
PVGLG_HSVE4	271-298					PVGLB_HSVEA	542-576	911-961					
PVGLG_HSVEB	383-410					PVGLB_HSVEB	542-576	911-961					
PVGLG_RABVT	489-519					PVGLB_HSVEL	542-576	910-960					
PVGLG_VSVIG	472-499					PVGLB_HSVMD	390-435	649-683	787-845				
PVGLH_EBV	549-578	619-648				PVGLB_HSVSA	240-288	406-447					
PVGLH_HCMVA	107-136	270-297				PVGLB_MCMV8	208-260	427-475	693-778	880-894			
PVGLH_HCMVT	106-135					PVGLB_PRVIF	847-881						
PVGLH_HSV6G	62-89	380-403				PVGLB_VZVD	92-133	596-630	809-867				
PVGLH_HSVSA	388-415					PVGLC_HSV11	469-510						
PVGLI_HCMVA	47-111					PVGLC_HSV1K	469-510						
PVGLM_BUNGE	512-546	914-941	1128-1255			PVGLC_HSV2	442-476						
PVGLM_BUNL7	813-950					PVGLC_HSV23	443-477						
PVGLM_BUNYW	340-374	504-535	682-709			PVGLC_HSVBC	235-269						

PVGLM_DUGBV	945-972					PVGLC_HSVEB	182-218					
PVGLM_HANTB	73-100	693-720				PVGLC_HSVMB	63-87					
PVGLM_HANTH	75-102					PVGLC_HSVMG	62-86					
PVGLM_HANTL	75-102					PVGLC_HSVMM	63-87					
PVGLM_HANTV	75-102					PVGLC_PRVIF	183-235					
PVGLM_PHV	69-96					PVGLC_VZVD	280-321					
PVGLM_PUUMH	72-110					PVGLC_VZVS	280-321					
PVGLM_PUUMS	72-110					PVGLD_HSVEA	89-123					
PVGLM_SEOUR	73-100	513-540	694-721			PVGLD_HSVEB	139-173					
PVGLM_SEOUS	73-100	513-540	694-721			PVGLD_HSVEK	139-173					
PVGLN_BEFV	523-564					PVGLE_HSV11	111-145					
PVGLP_BEV	48-82	1145-1179	1184-1211	1505-1532		PVGLE_HSV2	111-159					
PVGLX_HSVEB	17-44	413-444				PVGLF_BRSVA	146-202	504-545				
PVGLX_PRVRI	427-461					PVGLF_BRSVC	146-202	267-302	506-547			
PVGLY_JUNIN	14-41					PVGLF_BRSVR	146-202	267-302	506-554			
PVGLY_LASSG	88-113					PVGLF_CDVO	228-297	340-381	568-602			
PVGLY_MOPEI	86-113	316-346				PVGLF_HRSV1	116-203	267-302	506-549			
PVGLY_PIARV	334-375					PVGLF_HRSVA	116-202	267-302	506-549			
PVGLY_TACV	109-138	315-350				PVGLF_HRSVL	116-202	267-302	506-547			
PVGLY_TACV5	303-338					PVGLF_HRSVR	116-202	267-302	506-549			
PVGLY_TACV7	302-337					PVGLF_MEASE	116-184	228-269	452-500			
PVGLY_TACVT	303-338					PVGLF_MEASI	119-187	231-272	455-503			
PVGLZ_HSVEK	17-44					PVGLF_MEASY	116-184	228-269	452-500			
PVGNM_BPMV	403-430					PVGLF_MUMPM	20-54	103-179	235-272	447-502		
PVGNM_CPSMV	192-221					PVGLF_MUMPR	20-54	103-179	235-272	447-502		
PVGPS_EBV	104-149					PVGLF_MUMPS	20-54	103-179	235-272	447-502		
PVM1_REOVL	290-317					PVGLF_NDVA	117-182	231-272	426-512			
PVM21_REOVD	625-662					PVGLF_NDVB	122-182	231-272	426-517			
PVM22_REOVD	624-661					PVGLF_NDVI	133-182	238-272	426-517			
PVM2_REOVJ	624-661					PVGLF_NDVM	117-182	231-272	426-512			
PVM3_REOVD	159-186	343-370	456-483	631-660		PVGLF_NDVT	117-182	231-272	426-517			
PVMA2_BRSVA	124-152					PVGLF_NDVTG	122-182	231-272	426-517			
PVMA2_HRSVA	124-151					PVGLF_NDVU	122-182	231-272	426-512			
PVMAT_BRSVA	218-246					PVGLF_PHODV	28-63	187-266	309-350	533-581		
PVMAT_HRSVA	218-246					PVGLF_PI1HC	123-174	207-267	459-503			
PVMAT_INCJJ	151-185					PVGLF_PI2H	93-183	477-528				
PVMAT_NDVA	247-274					PVGLF_PI2HG	93-183	477-528				
PVMAT_PI2HT	98-123					PVGLF_PI2HT	93-185	477-528				
PVMAT_PI3B	201-231					PVGLF_PI3B	117-182	207-241	456-518			
PVMAT_PI3H4	201-231					PVGLF_PI3H4	117-182	207-241	462-532			
PVMAT_SV41	323-353					PVGLF_RINDK	112-180	224-265	448-493			
PVME1_CVBM	175-209					PVGLF_RINDL	112-180	224-265	448-506			
PVME1_CVTKE	175-209					PVGLF_SEND5	127-188	211-271	463-533			
PVME1_IBV6	21-48	184-218				PVGLF_SENDF	127-188	211-271	463-533			
PVME1_IBVB	21-48	184-218				PVGLF_SENDH	127-188	218-271	463-533			
PVME1_IBVB2	21-48	184-218				PVGLF_SENDJ	127-188	211-271	463-533			
PVME1_IBVK		184-218				PVGLF_SENDZ	127-188	211-271	463-533			

PVMP_CAMVC		220-254	273-324			PVGLF_6V41	96-186	454-508					
PVMP_CAMVD	29-56	220-254	273-324			PVGLF_6V5	103-171	241-275	451-487				
PVMP_CAMVE		227-254	273-324			PVGLF_TRTV	105-161	190-224	457-498				
PVMP_CAMVN		220-254	273-324			PVGLG_BEFV	508-612						
PVMP_CAMVS		220-254	273-324			PVGLG_BRSVC	30-70	104-138					
PVMP_CAMVW		220-254	273-324			PVGLG_HRSV1	30-81						
PVMP_CERV	26-53	100-127				PVGLG_HRSV2	30-85						
PVMP_SOCMV	4-31	78-118				PVGLG_HRSV3	30-85						
PVMSA_HPBHE	294-328					PVGLG_HRSV4	30-107						
PVMT1_DHVI1	38-85	237-284				PVGLG_HRSV5	30-85						
PVMT8_MYXVL	163-190					PVGLG_HRSV6	30-85						
PVMT9_MYXVL	465-492					PVGLG_HRSV7	30-85						
						PVGLG_HRSV8	30-81						
						PVGLG_HRSVA	30-67						
						PVGLG_HRSVL	25-65						
						PVGLG_HSVE4	271-305						
						PVGLG_SIGMA	344-381	464-498					
						PVGLG_SYNV	488-523						
						PVGLG_VHSV0	383-397						
						PVGLG_VSVIG	478-510						
						PVGLH_EBV	53-87	160-201	336-380	653-694			
						PVGLH_HCMVA	103-137	270-311	693-741				
						PVGLH_HCMVT	102-136	692-740					
						PVGLH_HSV11	447-481						
						PVGLH_HSV1E	447-481						
						PVGLH_HSV6G	357-406						
						PVGLH_HSVBC	364-416						
						PVGLH_HSVE4	334-379	414-455					
						PVGLH_HSVEB	327-372	407-448					
						PVGLH_HSVGA	32-66	374-453	664-712				
						PVGLH_MCMVS	440-474						
						PVGLH_PRVKA	226-260						
						PVGLH_PRVN3	226-260						
						PVGLH_PRVRI	226-260						
						PVGLH_VZVD	455-506						
						PVGLI_HCMVA	47-111	323-359					
						PVGLM_BUNGE	512-567	685-737	1228-1262				
						PVGLM_BUNL7	643-677	916-950					
						PVGLM_BUNSH	643-677						
						PVGLM_BUNYW	340-374	504-563	905-939				
						PVGLM_DUGBV	937-989	1239-1300					
						PVGLM_HANTB	693-727						
						PVGLM_HANTH	72-106						
						PVGLM_HANTL	72-106						
						PVGLM_HANTV	72-106						
						PVGLM_PHV	73-111						
						PVGLM_PTPV	149-251						

						PVGLM_SEOUR	694-728						
						PVGLM_SEOUS	693-730						
						PVGLN_BEFV	377-414	513-569					
						PVGLP_BEV	43-82	90-124	622-656	1128-1236			
						PVGLX_HSVEB	177-262						
						PVGLX_PRVRI	420-461						
						PVGLY_JUNIN	301-349						
						PVGLY_LASSG	317-360	388-422					
						PVGLY_LASSJ	318-361	389-423					
						PVGLY_LYCVA	333-367	395-432					
						PVGLY_LYCVW	124-168	333-367	395-432				
						PVGLY_MOPEI	316-359						
						PVGLY_PIARV	334-375						
						PVGLY_TACV	316-363						
						PVGLY_TACV5	303-351	382-416					
						PVGLY_TACV7	302-360	381-415					
						PVGLY_TACVT	303-351	382-416					
						PVGNB_CPMV	635-669						
						PVGNM_BPMV	143-177	403-437					
						PVGNM_CPMV	160-201						
						PVGNM_CPSMV	192-226	758-792	874-916				
						PVGNM_RCMV	837-871	912-946					
						PVGP8_EBV	94-149						
						PVM01_VACCC	5-56						
						PVM1_REOVL	287-321						
						PVM21_REOVD	416-450	619-663					
						PVM22_REOVD	416-450	618-662					
						PVM2_REOVJ	416-450	618-662					
						PVM2_REOVL	416-450	618-662					
						PVM3_REOVD	136-190	337-371	523-558	618-690			
						PVMA2_BRSVA	42-80						
						PVMA2_HRSVA	42-80						
						PVMAT_CDVO	193-234						
						PVMAT_INCJJ	73-114	151-208					
						PVMAT_NDVA	310-358						
						PVMAT_NDVB	324-358						
						PVMAT_PI3B	99-133	204-252					
						PVMAT_PI3H4	99-133	204-252					
						PVMAT_RABVA	69-103						
						PVMAT_RABVC	69-103						
						PVMAT_RABVE	69-103						
						PVMAT_RABVN	69-103						
						PVMAT_RABVP	69-103						
						PVMAT_RABVS	69-103						
						PVMAT_SYNV	246-280						
						PVMAT_VSVIG	198-232						
						PVME1_CVBM	175-209						

						PVME1_CVPFS	98-146	212-257						
						PVME1_CVPPU	212-257							
						PVME1_CVPRM	212-257							
						PVME1_CVTKE	28-62	175-209						
						PVME1_FIPV	212-257							
						PVME1_IBV6	21-55	177-218						
						PVME1_IBVB	21-55	177-218						
						PVME1_IBVB2	21-55	177-218						
						PVME1_IBVK	36-84							
						PVMP_CAMVC	187-254	270-324						
						PVMP_CAMVD	187-254	270-324						
						PVMP_CAMVE	187-254	270-324						
						PVMP_CAMVN	187-254	270-324						
						PVMP_CAMVS	187-254	270-324						
						PVMP_CAMVW	187-254	270-324						
						PVMP_CERV	212-248							
						PVMP_FMVD	217-251							
						PVMP_SOCMV	76-118							
						PVMSA_HPBDB	272-313	324-361						
						PVMSA_HPBDC	271-312	323-360						
						PVMSA_HPBDU	234-275	289-323						
						PVMSA_HPBDW	272-313	324-361						
						PVMSA_HPBGS	210-244							
						PVMSA_HPBHE	294-328							
						PVMSA_WHV1	208-242							
						PVMSA_WHV59	213-247							
						PVMSA_WHV7	213-247							
						PVMSA_WHVBI	213-247							
						PVMT1_DHVI1	201-235							
						PVMT1_IAANN	92-126	174-222						
						PVMT1_IABAN	92-126	174-222						
						PVMT1_IACAO	31-79							
						PVMT1_IAFOW	92-126	174-222						
						PVMT1_IAFPR	92-126	174-222						
						PVMT1_IAFPW	92-126	174-222						
						PVMT1_IALE1	92-126	174-222						
						PVMT1_IALE2	92-126	174-222						
						PVMT1_IAMAN	92-126	174-222						
						PVMT1_IAPOC	92-126	174-222						
						PVMT1_IAPUE	92-126	174-222						
						PVMT1_IAUDO	92-126	174-222						
						PVMT1_IAWIL	92-126	174-222						
						PVMT1_IAZI1	92-126	174-222						
						PVMT1_INBAC	175-209							
						PVMT1_INBAD	175-209							
						PVMT1_INBLE	175-209							
						PVMT1_INBSI	175-209							

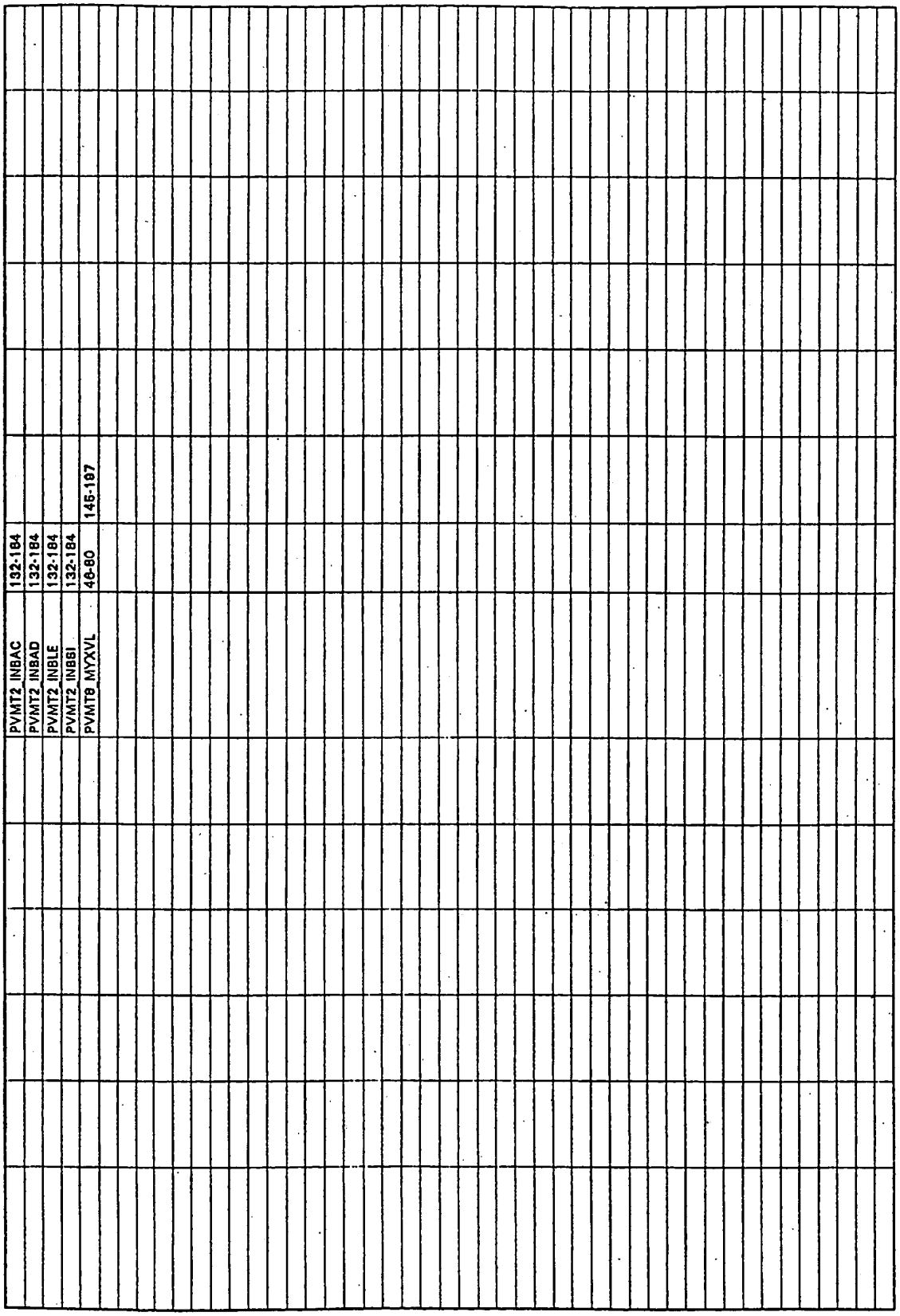
PVMT2_INBAC 132-184
PVMT2_INBAD 132-184
PVMT2_INBLE 132-184
PVMT2_INBBI 132-184
PVMT8_MYXVL 46-80 146-197

TABLE VI

Search Results Summary for PCTLZIP, P1CTLZIP, and P2CTLZIP Motifs

PCTLZIP			P1CTLZIP					P2CTLZIP			
LIBRARY FILE			LIBRARY FILE					LIBRARY FILE			
PENV_FOAMV	481-496		PENV_BIV06	434-450				PENV_BIV06	525-542		
PENV_HV1MA	438-453		PENV_BIV27	463-479				PENV_BIV27	554-571		
PENV_HV1MF	183-198		PENV_FOAMV	481-496	864-880			PENV_FENV1	30-47	630-647	
PENV_HV1RH	445-460		PENV_HV1KB	752-768				PENV_FIVPE	781-798		
PENV_HV1SC	186-201		PENV_HV1MA	437-453				PENV_FIVSD	778-796		
PENV_HV1Z2	123-138		PENV_HV1MF	183-198				PENV_FIVT2	780-797		
PENV_HV1ZH	438-453		PENV_HV1RH	444-460				PENV_FLVC6	38-55	624-641	
PENV_HV2BE	750-765		PENV_HV1S1	738-754				PENV_FLVGL	605-622		
PENV_HV2D1	741-756		PENV_HV1SC	186-201				PENV_FLVLB	625-642		
PENV_HV2G1	741-756		PENV_HV1Z2	123-138				PENV_FLVSA	602-619		
PENV_HV2NZ	742-757		PENV_HV1Z3	117-133				PENV_FOAMV	710-727	957-974	
PENV_HV2RO	751-766		PENV_HV1ZH	437-453				PENV_FSVGA	625-642		
PENV_HV2SB	743-758		PENV_HV2BE	750-765				PENV_FSVGB	605-622		
PENV_HV2ST	745-760		PENV_HV2D1	741-756				PENV_FSVSM	608-625		
PENV_JSRV	104-119		PENV_HV2G1	741-756				PENV_HV1OY	123-140		
PENV_MMTVB	618-633		PENV_HV2NZ	742-757				PENV_HV1Z2	410-427		
PENV_MMTVG	618-633		PENV_HV2RO	751-766				PENV_HV1Z3	154-171		
PENV_SIVMK	139-154		PENV_HV2SB	743-758				PENV_HV2CA	750-767		
PENV_SIVML	139-154		PENV_HV2ST	745-760				PENV_MCFF	600-617		
PHEMA_CVBLY	391-408		PENV_JSRV	104-119	541-557			PENV_MCFF3	601-618		
PHEMA_CVBM	391-408		PENV_MCFF	397-413				PENV_MLVAV	630-647		
PHEMA_CVBQ	391-408		PENV_MCFF3	397-413				PENV_MLVCB	625-642		
PHEMA_CVHOC	391-408		PENV_MLVAV	427-443				PENV_MLVF5	639-656		
PHEMA_CVMA5	402-417		PENV_MLVCB	422-438				PENV_MLVFF	639-656		
PHEMA_CVMS	403-418		PENV_MLVHO	423-439				PENV_MLVFP	639-656		
PHEMA_INBAA	295-310		PENV_MLVMO	426-442				PENV_MLVHO	626-643		
PHEMA_INBBE	303-318		PENV_MLVRD	424-440				PENV_MLVKI	167-184		
PHEMA_INBBO	293-308		PENV_MLVRK	424-440				PENV_MLVMO	629-646		
PHEMA_INBEN	301-316		PENV_MMTVB	618-633				PENV_MLVRD	624-641		
PHEMA_INBFU	286-301		PENV_MMTVG	618-633				PENV_MLVRK	624-641		
PHEMA_INBGL	296-311		PENV_SFV1	864-880				PENV_MSVFB	170-187		
PHEMA_INBHK	283-308		PENV_SFV3L	861-877				PENV_RMCFV	603-620		
PHEMA_INBIB	288-303		PENV_SIVGB	93-109				PENV_SFV1	710-727	957-974	
PHEMA_INBID	299-314		PENV_SIVMK	139-154	802-818			PENV_SFV3L	707-724	954-971	
PHEMA_INBLE	302-317		PENV_SIVML	139-154	801-817			PENV_SIVM1	766-783		
PHEMA_INBMD	292-307		PENV_SIVS4	808-822				PENV_SIVMK	765-782		
PHEMA_INBME	296-311		PENV_SIVSP	810-826				PENV_SIVML	764-781		
PHEMA_INBNA	288-303		PHEMA_CDVO	36-52				PENV_SIVS4	769-786		
PHEMA_INBOR	301-316		PHEMA_CVBLY	391-408				PENV_SIVSP	773-790		
PHEMA_INBSI	301-316		PHEMA_CVBM	391-408				PENV_SMRVH	536-553		
PHEMA_INBSJ	296-313		PHEMA_CVBQ	391-408				PENV_SM9AV	42-59		
PHEMA_INBUS	294-309		PHEMA_CVHOC	391-408				PHEMA_CDVO	36-53	200-217	
PHEMA_INBVI	296-311		PHEMA_CVMA5	402-417				PHEMA_CVBLY	391-408		
PHEMA_INBVK	303-318		PHEMA_CVMS	403-418				PHEMA_CVBM	391-408		
PHEMA_INBYB	286-301		PHEMA_IAAIC	237-253				PHEMA_CVBQ	391-408		

PHEMA_MUMPM	133-148		PHEMA_IABAN	221-237				PHEMA_CVHOC	391-408		
PHEMA_MUMPR	133-148		PHEMA_IABUD	234-250				PHEMA_IAAIC	322-339		
PHEMA_MUMPS	133-148		PHEMA_IACKA	234-250				PHEMA_IABAN	306-323		
PHEMA_PI1HW	345-360		PHEMA_IACKG	231-247				PHEMA_IABUD	320-337		
PHEMA_PI2H	65-80		PHEMA_IACKV	230-246				PHEMA_IACKA	320-337		
PHEMA_PI2HT	65-80		PHEMA_IADA1	234-250				PHEMA_IACKG	316-333		
PHEMA_RINDK	368-383		PHEMA_IADA3	237-253				PHEMA_IACKP	302-319		
PHEMA_SV5	7-94		PHEMA_IADCZ	234-250				PHEMA_IACKQ	302-319		
PHEMA_SV5CM	7-94		PHEMA_IADH1	221-237				PHEMA_IACKS	319-336		
PHEMA_SV5CP	7-94		PHEMA_IADH2	221-237				PHEMA_IACKV	315-332		
PHEMA_SV5LN	7-94		PHEMA_IADH3	221-237				PHEMA_IADA1	320-337		
PVENV_DHVI1	42-57		PHEMA_IADH4	221-237				PHEMA_IADA3	322-339		
PVFP7_CAPVK	89-104		PHEMA_IADH5	221-237				PHEMA_IADCZ	320-337		
PVFUS_VACCS	72-87		PHEMA_IADH6	221-237				PHEMA_IADH1	306-323		
PVG01_BPP22	242-257		PHEMA_IADH7	221-237				PHEMA_IADH2	306-323		
PVG01_HSVEB	169-184		PHEMA_IADM2	237-253				PHEMA_IADH3	306-323		
PVG01_HSVI1	210-225	317-332	PHEMA_IADNZ	234-250				PHEMA_IADH4	306-323		
PVG06_BPT4	184-199		PHEMA_IAEN6	221-237				PHEMA_IADH6	306-323		
PVG07_BPT4	885-900		PHEMA_IAEN7	237-253				PHEMA_IADH7	306-323		
PVG08_HSVI1	134-149		PHEMA_IAFPR	230-246				PHEMA_IADM2	322-339		
PVG10_BPPH2	183-198		PHEMA_IAHAL	236-252				PHEMA_IADNZ	320-337		
PVG10_BPPZA	183-198		PHEMA_IAHAR	235-251				PHEMA_IADU3	322-339		
PVG10_HSVSA	109-124		PHEMA_IAHC6	230-246				PHEMA_IAEN6	306-323		
PVG16_BPP1	81-96		PHEMA_IAHC7	230-246				PHEMA_IAEN7	322-339		
PVG16_BPT4	466-483		PHEMA_IAHCD	230-246				PHEMA_IAFPR	315-332		
PVG25_BPT4	97-112		PHEMA_IAHDE	230-246				PHEMA_IAGRE	320-337		
PVG29_HSVI1	20-35		PHEMA_IAHFO	236-252				PHEMA_IAGU2	320-337		
PVG30_BPPH6	11-94		PHEMA_IAHK6	236-252				PHEMA_IAGUA	319-336		
PVG36_BPOX2	22-37		PHEMA_IAHK7	236-252				PHEMA_IAHAL	321-338		
PVG36_HSV6A	108-123		PHEMA_IAHLE	230-246				PHEMA_IAHC6	315-332		
PVG37_BPT2	1253-1268		PHEMA_IAHLO	230-246				PHEMA_IAHC7	315-332		
PVG37_HSVI1	284-299		PHEMA_IAHMI	236-252				PHEMA_IAHCD	315-332		
PVG55_HSVI1	22-37	143-158	PHEMA_IAHNM	236-252				PHEMA_IAHDE	315-332		
PVG56_HSVI1	268-283		PHEMA_IAHRO	236-252				PHEMA_IAHFO	321-338		
PVG56_HSVI1	102-117		PHEMA_IAHSA	236-252				PHEMA_IAHK6	321-338		
PVG59_HSVI1	267-282		PHEMA_IAHSP	230-246				PHEMA_IAHK7	321-338		
PVG65_HSVI1	516-533		PHEMA_IAHSW	230-246				PHEMA_IAHLE	315-332		
PVG9_BPPH2	234-249		PHEMA_IAHTE	236-252				PHEMA_IAHLO	315-332		
PVG9_BPPZA	234-249		PHEMA_IAHTO	236-252				PHEMA_IAHMI	321-338		
PVG9_SPV1R	57-72		PHEMA_IAHUR	236-252				PHEMA_IAHNM	321-338		
PVGF_BPPHX	234-249		PHEMA_IAKIE	235-251				PHEMA_IAHNN	315-332		
PVGL2_CVBF	264-279		PHEMA_IALEN	235-251				PHEMA_IAHPR	315-332		
PVGL2_CVBL9	264-279		PHEMA_IAMAA	233-249				PHEMA_IAHRO	321-338		
PVGL2_CVBLY	264-279		PHEMA_IAMAB	238-254				PHEMA_IAHSA	321-338		
PVGL2_CVBM	264-279		PHEMA_IAMAO	237-253				PHEMA_IAHSP	315-332		
PVGL2_CVBQ	264-279		PHEMA_IAME1	237-253				PHEMA_IAHSW	315-332		
PVGL2_CVBV	264-279		PHEMA_IAME2	237-253				PHEMA_IAHTE	321-338		

PVGL2_CVPFS	442-467		PHEMA_IAME6	221-237				PHEMA_IAHTO	321-338		
PVGL2_CVPPU	440-466	504-519	PHEMA_IAMIN	85-101	231-247			PHEMA_IAHUR	321-338		
PVGL2_CVPR8	218-233		PHEMA_IANT6	237-253				PHEMA_IAJAP	317-334		
PVGL2_CVPRM	218-233		PHEMA_IAQU7	221-237				PHEMA_IAMAA	319-336		
PVGL2_IBV6	1056-1071		PHEMA_IARUD	234-250				PHEMA_IAMAB	324-341		
PVGL2_IBVB	1055-1070		PHEMA_IASE2	234-250				PHEMA_IAMAO	322-339		
PVGL2_IBVD2	1056-1071		PHEMA_IASH2	234-250				PHEMA_IAME1	322-339		
PVGL2_IBVK	1055-1070		PHEMA_IASTA	230-246				PHEMA_IAME2	322-339		
PVGL2_IBVM	1056-1070		PHEMA_IATAI	235-251				PHEMA_IAME6	306-323		
PVGLB_HSVSA	701-716		PHEMA_IATKM	234-250				PHEMA_IAMIN	316-333		
PVGLB_PRVIF	203-218		PHEMA_IATKO	233-249				PHEMA_IANT6	322-339		
PVGLC_HSVBC	475-490		PHEMA_IATKR	230-246				PHEMA_IAPIL	320-337		
PVGLC_HSVE4	444-459		PHEMA_IATKW	229-245				PHEMA_IAQU7	306-323		
PVGLC_HSVEB	427-442		PHEMA_IAUDO	237-253				PHEMA_IARUD	320-337		
PVGLC_PRVIF	446-461		PHEMA_IAUS9	235-251				PHEMA_IASE2	320-337		
PVGLD_HSV11	79-94		PHEMA_IAVI7	238-254				PHEMA_IASH2	321-338		
PVGLD_HSV2	79-94		PHEMA_IAXIA	235-251				PHEMA_IASTA	315-332		
PVGLF_BR6VA	265-280		PHEMA_IAZCO	237-253				PHEMA_IATKM	320-337		
PVGLF_BRSVC	265-280		PHEMA_IAZH2	221-237				PHEMA_IAUDO	322-339	380-397	
PVGLF_BRSVR	265-280		PHEMA_IAZH3	221-237				PHEMA_IAVI7	323-340		
PVGLF_HR8V1	265-280		PHEMA_IAZUK	237-253				PHEMA_IAZCO	322-339		
PVGLF_HR6VA	265-280		PHEMA_INBAA	115-131	285-310			PHEMA_IAZH2	306-323		
PVGLF_HRSVL	265-280		PHEMA_INBBE	123-139	303-318			PHEMA_IAZH3	306-323		
PVGLF_HRSVR	265-280		PHEMA_INBBO	116-132	293-308			PHEMA_IAZUK	322-339		
PVGLF_MUMPS	5-94		PHEMA_INBEN	123-139	301-316			PHEMA_MUMPM	101-118		
PVGLI_VZVD	278-293		PHEMA_INBFU	108-124	286-301			PHEMA_MUMPR	101-118		
PVGLM_HANTB	900-915		PHEMA_INBGL	119-135	296-311			PHEMA_MUMPS	101-118		
PVGLM_PTPV	743-758		PHEMA_INBHK	116-132	293-308			PHEMA_NDVA	93-110		
PVGLM_SEOUR	901-916		PHEMA_INBIB	108-124	288-303			PHEMA_NDVB	93-110		
PVGLM_SEOUS	900-915		PHEMA_INBID	120-136	299-314			PHEMA_NDVD	93-110		
PVGLY_LASSG	426-441		PHEMA_INBLE	123-139	302-317			PHEMA_NDVH	93-110		
PVGLY_LASSJ	427-442		PHEMA_INBMD	113-129	292-307			PHEMA_NDVI	93-110		
PVGLY_MOPEI	425-440		PHEMA_INBME	116-132	296-311			PHEMA_NDVM	93-110		
PVM3_REOVD	521-536		PHEMA_INBNA	108-124	288-303			PHEMA_NDVQ	93-110		
PVMSA_HPBG9	380-395		PHEMA_INBOR	123-139	301-316			PHEMA_NDVTG	93-110		
PVMSA_HPBV9	187-202		PHEMA_INBSI	123-139	301-316			PHEMA_NDVU	93-110		
PVMSA_WHV1	378-393		PHEMA_INBSJ	119-135	298-313			PHEMA_PHODV	36-53		
PVMSA_WHV59	383-398		PHEMA_INBUS	116-132	294-309			PHEMA_PI1HW	486-503		
PVMSA_WHV7	383-398		PHEMA_INBVI	116-132	296-311			PHEMA_PI3B	111-128		
PVMSA_WHV8	383-398		PHEMA_INBVK	123-139	303-318			PHEMA_PI3H4	111-128		
PVMSA_WHV8I	383-398		PHEMA_INBYB	108-124	286-301			PHEMA_PI3HA	111-128		
PVMSA_WHVW8	234-249		PHEMA_MUMPM	133-148				PHEMA_PI3HT	111-128		
PVMT2_IAANN	25-40		PHEMA_MUMPR	133-148				PHEMA_PI3HU	111-128		
PVMT2_IABAN	25-40		PHEMA_MUMPS	133-148				PHEMA_PI3HV	111-128		
PVMT2_IAFOW	25-40		PHEMA_PI1HW	345-360				PHEMA_PI3HW	111-128		
PVMT2_IAFPR	25-40		PHEMA_PI2H	65-81				PHEMA_PI3HX	111-128		
PVMT2_IAFPW	25-40		PHEMA_PI2HT	65-81				PHEMA_PI4HA	50-67		

PVMT2_IALE1	25-40		PHEMA_PI3B	324-340				PHEMA_SV41	85-102		
PVMT2_IALE2	25-40		PHEMA_PI3H4	324-340				PHEMA_SV5	84-101		
PVMT2_IAMAN	25-40		PHEMA_PI3HA	324-340				PHEMA_SV5CM	84-101		
PVMT2_IAPUE	25-40		PHEMA_PI3HT	324-340				PHEMA_SV5CP	84-101		
PVMT2_IASIN	25-40		PHEMA_PI3HU	324-340				PHEMA_SV5LN	84-101		
PVMT2_IAUDO	25-40		PHEMA_PI3HV	324-340				PVF05_VACCC	280-297		
PVMT2_IAWIL	25-40		PHEMA_PI3HW	324-340				PVF05_VACCP	280-297		
PVMT9_MYXVL	226-241		PHEMA_PI3HX	324-340				PVF05_VACCV	281-298		
			PHEMA_RINDK	368-383				PVF09_VACCC	176-193		
			PHEMA_SV5	7-94				PVF09_VACCV	176-193		
			PHEMA_SV5CM	7-94				PVG27_HSVSA	209-226		
			PHEMA_SV5CP	7-94				PVG28_HSVI1	173-190		
			PHEMA_SV5LN	7-94				PVG39_HSVI1	648-665		
			PVENV_DHVI1	42-57				PVG43_HSVI1	109-126	521-538	
			PVENV_EAV	25-41				PVG67_HSVI1	171-188		
			PVFP2_FOWPV	88-104				PVG72_HSVI1	1252-1269		
			PVFP7_CAPVK	89-104				PVGF1_IBVB	3073-3090		
			PVFUS_VACC6	72-87				PVGL2_IBV6	1094-1111		
			PVG01_HSVEB	169-184				PVGLB_HSVE1	736-753		
			PVG01_HSVI1	209-225	317-332			PVGLB_HSVE4	675-692		
			PVG08_HSVI1	134-149				PVGLB_HSVEA	736-753		
			PVG10_HSV6A	109-124				PVGLB_HSVEB	736-753		
			PVG11_HSVI1	103-119				PVGLB_HSVEL	736-753		
			PVG12_HSVI1	270-286				PVGLB_ILTV6	597-614		
			PVG1_SPV1R	76-92				PVGLB_ILTV8	607-624		
			PVG29_HSVI1	20-35				PVGLB_ILTVT	607-624		
			PVG36_BPOX2	22-37				PVGLC_PRVIF	180-197		
			PVG36_HSV6A	108-123				PVGLE_VZVD	469-486		
			PVG37_HSVI1	284-299				PVGLF_SV5	401-418		
			PVG41_HSVI1	244-260				PVGLH_HCMVA	365-382		
			PVG46_HSVI1	1244-1260				PVGLH_HCMVT	364-381		
			PVG55_HSVI1	22-37	143-158			PVGLH_HSV11	245-262	803-820	
			PVG56_HSVI1	268-283				PVGLH_HSV1E	245-262	803-820	
			PVG58_HSVI1	101-117				PVGLI_HSV11	43-60		
			PVG58_HSVSA	130-146	330-346			PVGLM_BUNL7	81-98		
			PVG59_HSVI1	267-282				PVGLM_BUNSH	81-98		
			PVG65_HSVI1	362-378	518-533			PVGLM_PUUMH	712-729		
			PVG71_HSV6A	89-105				PVGLM_PUUMS	712-729		
			PVG9_BPPH2	234-249				PVGLM_RVFV	344-361		
			PVG9_BPPZA	234-249				PVGLM_RVFVZ	344-361		
			PVG9_SPV1R	57-72				PVGLY_LASSG	12-94		
			PVGF1_IBVB	2210-2226				PVGLY_LASSJ	12-94		
			PVGL2_CVBF	123-139	174-190	264-279		PVGLY_LYCVA	12-94		
			PVGL2_CVBL9	123-139	174-190	264-279		PVGLY_LYCVW	12-94		
			PVGL2_CVBLY	123-139	174-190	264-279		PVGLY_MOPEI	12-94		
			PVGL2_CVBM	123-139	174-190	264-279		PVM1_REOVD	280-297		
			PVGL2_CVBQ	31-47	123-139	174-190	264-279	PVM1_REOVL	280-297		

			PVGL2_CVBV	123-139	174-190	264-279		PVMAT_CDVO	148-165		
			PVGL2_CVM4	95-111	1267-1283			PVMAT_MEASI	87-104		
			PVGL2_CVMA5	95-111	1215-1231			PVMP_CAMVC	147-164		
			PVGL2_CVMJH	95-111	1126-1142			PVMP_CAMVD	147-164		
			PVGL2_CVPFS	442-457	800-816	1274-1290		PVMP_CAMVE	147-164		
			PVGL2_CVPPU	440-455	504-519	788-814	1272-1288	PVMP_CAMVN	147-164		
			PVGL2_CVPR8	218-233	576-592	1050-1066		PVMP_CAMVS	147-164		
			PVGL2_CVPRM	218-233	576-592	1050-1066		PVMP_CAMVW	147-164		
			PVGL2_FIPV	803-819	1277-1293			PVMSA_HPBV0	11-94		
			PVGL2_IBV6	1056-1071				PVMSA_HPBV2	185-202		
			PVGL2_IBVB	1055-1070				PVMSA_HPBV4	185-202		
			PVGL2_IBVD2	1056-1071				PVMSA_HPBVA	174-191		
			PVGL2_IBVK	1055-1070				PVMSA_HPBVD	11-94		
			PVGL2_IBVM	1055-1070				PVMSA_HPBVJ	174-191		
			PVGLB_HSV8A	701-716				PVMSA_HPBVL	174-191		
			PVGLB_PRVIF	203-218				PVMSA_HPBVN	11-94		
			PVGLB_VZVD	522-538				PVMSA_HPBVO	174-191		
			PVGLC_HSVBC	475-490				PVMSA_HPBVP	185-202		
			PVGLC_HSVE4	444-459				PVMSA_HPBVR	185-202		
			PVGLC_HSVEB	427-442				PVMSA_HPBVS	11-94		
			PVGLC_PRVIF	446-461				PVMSA_HPBVW	174-191		
			PVGLC_VZVD	150-166				PVMSA_HPBVY	174-191		
			PVGLC_VZVS	150-166				PVMSA_HPBVZ	174-191		
			PVGLD_HSV11	79-94				PVMT2_IAANN	25-42		
			PVGLD_HSV2	79-94				PVMT2_IABAN	25-42		
			PVGLE_PRVRI	3-94				PVMT2_IAFOW	25-42		
			PVGLF_BRSVA	205-221	265-280			PVMT2_IAFPR	25-42		
			PVGLF_BRSVC	205-221	265-280			PVMT2_IAFPW	25-42		
			PVGLF_BRSVR	205-221	265-280			PVMT2_IALE1	25-42		
			PVGLF_CDVO	398-414				PVMT2_IALE2	25-42		
			PVGLF_HRSV1	205-221	265-280			PVMT2_IAMAN	25-42		
			PVGLF_HRSVA	205-221	265-280			PVMT2_IAPUE	25-42		
			PVGLF_HRSVL	205-221	265-280			PVMT2_IASIN	25-42		
			PVGLF_HRSVR	205-221	265-280			PVMT2_IAUDO	25-42		
			PVGLF_MEASE	286-302				PVMT2_IAWIL	25-42		
			PVGLF_MEASI	289-305							
			PVGLF_MEASY	286-302							
			PVGLF_MUMPM	276-292							
			PVGLF_MUMPR	276-292							
			PVGLF_MUMPS	5-94	276-292						
			PVGLF_NDVA	273-289							
			PVGLF_NDVB	273-289							
			PVGLF_NDVM	273-289							
			PVGLF_NDVT	273-289							
			PVGLF_NDVTG	273-289							
			PVGLF_NDVU	273-289							
			PVGLF_PHODV	269-285	367-383						

			PVGLF_RINDK	282-298						
			PVGLF_RINDL	282-298						
			PVGLF_TRTV	175-191						
			PVGLI_VZVD	278-293						
			PVGLM_HANTB	355-371	900-915					
			PVGLM_HANTH	499-515						
			PVGLM_HANTL	499-515						
			PVGLM_HANTV	499-515						
			PVGLM_PTRV	743-758						
			PVGLM_PUUMH	509-525						
			PVGLM_PUUMS	509-525						
			PVGLM_SEOUR	355-371	901-916					
			PVGLM_SEOUS	355-371	900-915					
			PVGLM_UUK	826-842						
			PVGLP_BEV	869-885						
			PVGLY_LASSG	12-94	426-441					
			PVGLY_LASSJ	12-94	427-442					
			PVGLY_LYCVA	12-94						
			PVGLY_LYCVW	12-94						
			PVGLY_MOPEI	12-94	425-440					
			PVGLY_PIARV	12-94						
			PVGNM_CPMV	1021-1037						
			PVM3_REOVD	521-536						
			PVMAT_MUMPS	191-207						
			PVMAT_NDVA	135-151						
			PVMAT_NDVB	135-151						
			PVMAT_PI2HT	189-205						
			PVMAT_SV41	189-205						
			PVMAT_SV5	98-114	132-148					
			PVMP_CAMVC	118-134						
			PVMP_CAMVD	118-134						
			PVMP_CAMVE	118-134						
			PVMP_CAMVN	118-134						
			PVMP_CAMVS	118-134						
			PVMP_CAMVW	118-134						
			PVMP_FMVD	115-131						
			PVMSA_HPBGS	380-395						
			PVMSA_HPBV9	187-202						
			PVMSA_WHV1	378-393						
			PVMSA_WHV59	383-398						
			PVMSA_WHV7	383-398						
			PVMSA_WHV8	383-398						
			PVMSA_WHV8I	383-398						
			PVMSA_WHVW6	234-249						
			PVMT2_IAANN	25-40						
			PVMT2_IABAN	25-40						
			PVMT2_IAFOW	25-40						

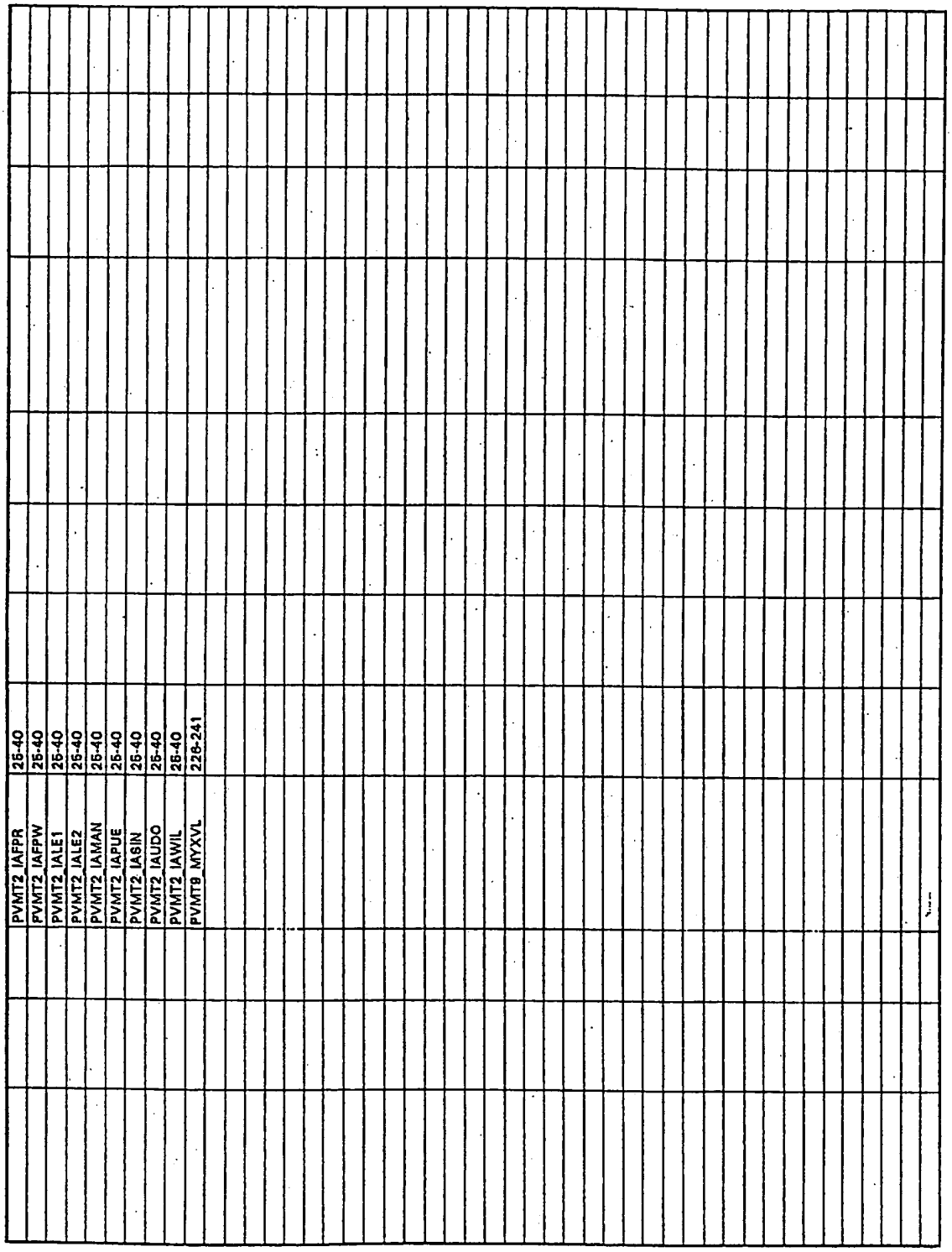
PVMT2_IAFPR 26-40
PVMT2_IAFPW 26-40
PVMT2_IALE1 26-40
PVMT2_IALE2 26-40
PVMT2_IAMAN 26-40
PVMT2_IAPUE 26-40
PVMT2_IASIN 26-40
PVMT2_IAUDO 26-40
PVMT2_IAWIL 26-40
PVMT9_MYXVL 226-241

TABLE VII

Search Results Summary for P3CTLZIP, P4CTLZIP, P5CTLZIP, and P6CTLZIP Motifs

P3CTLZIP			P4CTLZIP			P5CTLZIP			P6CTLZIP			
LIBRARY FILE			LIBRARY FILE			LIBRARY FILE			LIBRARY FILE			
PENV_BIV27	147-165		PENV1_FRSFV	380-399		PENV1_FRSFV	380-400		PENV_BIV06	47-66	626-646	
PENV_CAEVC	810-828		PENV_AVISU	98-117		PENV2_FRSFV	380-400		PENV_BIV27	47-66	147-166	564-575
PENV_CAEVG	808-826		PENV_BIV27	147-166		PENV_BAEVM	170-190		PENV_FENV1	226-246	630-651	
PENV_HV2BE	750-768		PENV_HV1ZH	123-142		PENV_FIVPE	781-801		PENV_FLVC6	624-645		
PENV_HV2D1	741-759		PENV_HV2D2	9-29		PENV_FIVSD	779-799		PENV_FLVGL	447-466	605-626	
PENV_HV2G1	741-759		PENV_HV2SB	778-797		PENV_FIVT2	780-800		PENV_FLVLB	467-486	625-646	
PENV_HV2NZ	742-760		PENV_JSRV	541-560		PENV_FLVGL	9-29		PENV_FLVSA	444-465	602-623	
PENV_HV2RO	751-769		PENV_RSVP	533-552		PENV_FOAMV	265-275	924-944	PENV_FOAMV	153-174	957-978	
PENV_HV2SB	743-761		PHEMA_VACCC	173-192		PENV_FSVGA	9-29		PENV_FSVGA	467-486	625-646	
PENV_HV2ST	745-763		PHEMA_VACCI	173-192		PENV_HV1C4	428-448		PENV_FSVGB	447-466	605-626	
PENV_JSRV	376-394		PHEMA_VACCT	173-192		PENV_HV2CA	750-770		PENV_FSVSM	450-471	608-629	
PHEMA_PI2H	118-136		PHEMA_VACCV	173-192		PENV_MLVF5	400-420		PENV_FSVST	467-486		
PHEMA_PI2HT	118-136		PVENV_BEV	62-81		PENV_MMTVB	643-663		PENV_GALV	52-73	619-640	
PHEMA_SV41	55-73		PVENV_MCV1	61-80		PENV_MMTVG	643-663		PENV_HV2BE	750-771		
PVENV_THOGV	473-491		PVENV_MCV2	61-80		PENV_OMVVS	75-95		PENV_HV2G1	741-762		
PVG16_BPP22	83-101		PVFUS_ORFNZ	29-48		PENV_RSVP	42-62		PENV_HV2NZ	742-763		
PVG24_BPT4	116-133		PVG01_HSVEB	169-188		PENV_SFV1	924-944		PENV_HV2RO	751-772		
PVG38_HSVSA	344-362		PVG01_VACCC	376-395		PENV_SFV3L	921-941		PENV_HV2ST	745-766		
PVG40_HSVI1	14-32		PVG01_VACCV	315-334		PENV_SIVM1	766-786		PENV_MCFF	600-621		
PVG50_HSVSA	5-24		PVG01_VARV	376-395		PENV_SIVMK	765-785		PENV_MCFF3	601-622		
PVG51_BPT4	63-81		PVG06_BPT4	627-646		PENV_SIVML	764-784		PENV_MLVAV	630-651		
PVG51_HSVI1	84-102		PVG10_HSVI1	35-54		PENV_SIVS4	769-789		PENV_MLVCB	625-646		
PVG65_HSVI1	155-173		PVG11_HSVI1	103-122	150-169	PENV_SIVSP	773-793		PENV_MLVF5	639-660		
PVGF1_IBVB	2788-2806	3374-3392	PVG1_BPPH2	31-50		PHEMA_CDVO	493-513		PENV_MLVFF	639-660		
PVGL2_CVH22	1053-1071		PVG1_SPV1R	659-678		PHEMA_CVBLY	391-411		PENV_MLVFP	639-660		
PVGL2_IBV6	1056-1074		PVG20_BPT4	231-250		PHEMA_CVBM	391-411		PENV_MLVHO	626-647		
PVGL2_IBVB	1055-1073		PVG32_VZVD	90-109		PHEMA_CVBQ	391-411		PENV_MLVKI	167-188		
PVGL2_IBVD2	1056-1074		PVG36_BPK3	132-151		PHEMA_CVHOC	391-411		PENV_MLVMO	629-650		
PVGL2_IBVK	1055-1073		PVG37_BPT2	19-38	629-648	PHEMA_CVMA5	402-422		PENV_MLVRD	624-645		
PVGL2_IBVM	1055-1073		PVG37_BPT4	19-38	625-644	PHEMA_IACKG	81-101		PENV_MLVRK	624-645		
PVGLB_HSVB1	680-678	689-707	PVG39_HSVI1	1038-1057		PHEMA_IADMA	81-101		PENV_MSVFB	170-191		
PVGLB_HSVBC	692-710		PVG41_HSVI1	62-81		PHEMA_MUMPM	397-417		PENV_RMCFV	603-624		
PVGLB_HSVSA	684-602		PVG43_BPPF3	380-399		PHEMA_MUMPR	397-417		PENV_SFV1	957-978		
PVGLB_ILTV6	740-758		PVG46_BPPF1	337-356		PHEMA_MUMPS	397-417		PENV_SFV3L	157-178	954-975	
PVGLB_ILTV9	750-768		PVG59_HSVI1	142-161		PHEMA_PHODV	493-513		PENV_SIVA1	437-458		
PVGLB_ILTVT	750-768		PVG61_HSVI1	117-136		PHEMA_PI1HW	322-342		PENV_SIVAG	442-463		
PVGLC_VZVD	431-449		PVG67_HSVI1	316-337	1072-1091	PHEMA_PI2H	13-33		PENV_SIVAI	421-442		
PVGLC_VZVS	431-449		PVGF1_IBVB	1587-1606	2108-2127	PHEMA_PI2HT	13-33		PENV_SIVAT	435-456		
PVGLF_PI3H4	2-94		PVGL2_CVBF	991-1010		PHEMA_RINDL	497-517		PENV_SM9AV	42-63		
PVGLH_HSV6G	314-332		PVGL2_CVBL9	991-1010		PHEMA_SEND5	322-342		PHEMA_CVMA5	402-423		
PVGLH_HSVE4	814-832		PVGL2_CVBLY	991-1010		PHEMA_SENDF	322-342		PHEMA_IADE1	266-287		
PVGLH_HSVEB	807-825		PVGL2_CVBM	991-1010		PHEMA_SENDH	322-342		PHEMA_MUMPM	225-246		
PVGLI_HSV11	5-24		PVGL2_CVBQ	991-1010		PHEMA_SENDJ	322-342		PHEMA_MUMPR	225-246		
PVGNM_BPMV	678-696		PVGL2_CVBV	991-1010		PHEMA_SENDZ	322-342		PHEMA_MUMPS	225-246		
PVM01_VACCC	134-152	177-195	PVGL2_CVH22	768-787	1115-1134	PVENV_LELV	27-47	148-168	PHEMA_PHODV	213-234		

PVM01_VACCV	83-101	126-144	PVGL2_CVM4	999-1018		PVENV_THOGV	356-376		PHEMA_PI2H	13-34		
PVM1_REOVD	227-245		PVGL2_CVMA5	947-966		PVG01_VACCC	298-318		PHEMA_PI2HT	13-34		
PVM1_REOVL	227-245		PVGL2_CVMJH	858-877		PVG01_VACCV	237-257		PHEMA_SV5	7-28	378-400	
PVMAT_HRSVA	44-62		PVGL2_CVPF5	64-83	1038-1057	PVG01_VARV	298-318		PHEMA_SV5CM	7-28	378-400	
PVMAT_NDVA	190-208		PVGL2_CVPPU	64-83	1036-1055	PVG06_VACCC	31-51		PHEMA_SV5CP	7-28	378-400	
PVMAT_NDVB	190-208		PVGL2_CVPRB	814-833		PVG06_VARV	31-51		PHEMA_SV5LN	7-28	378-400	
PVMP_CAMVC	183-201		PVGL2_CVPRM	814-833		PVG09_BPPF1	25-45		PVG01_HSVEB	169-190		
PVMP_CAMVD	183-201		PVGL2_FIPV	1041-1060		PVG12_HSVI1	161-171		PVG01_HSVI1	589-610		
PVMP_CAMVE	183-201		PVGL2_IBV6	588-607	771-790	PVG22_HSVI1	300-320		PVG23_HSVI1	314-335		
PVMP_CAMVN	183-201		PVGL2_IBVB	587-606	770-789	PVG39_HSVI1	648-668	970-990	PVG37_BPOX2	65-86		
PVMP_CAMVS	183-201		PVGL2_IBVD2	588-607	771-790	PVG51_HSVI1	29-49		PVG43_HSVI1	157-178		
PVMP_CAMVW	183-201		PVGL2_IBVK	587-606	770-789	PVG63_HSVI1	338-358		PVG55_HSVI1	288-309		
PVMP_FMVD	180-198		PVGL2_IBVM	587-606	770-789	PVG65_HSVI1	117-137		PVG56_HSV8A	85-106		
			PVGLB_HCMVA	706-725		PVG74_HSV8A	124-144		PVG58_HSVI1	1165-1176		
			PVGLB_HCMVT	707-726		PVGL2_IBV6	328-348		PVG58_HSV8A	266-287		
			PVGLB_HSV6U	117-136		PVGL2_IBVB	327-347		PVG60_HSVI1	30-51		
			PVGLB_ILTV6	256-275		PVGL2_IBVD2	328-348		PVG63_HSVI1	238-259		
			PVGLB_ILTVS	266-285		PVGL2_IBVD3	328-348		PVGF1_IBVB	1856-1877		
			PVGLB_ILTVT	266-285		PVGL2_IBVK	327-347		PVGH3_HCMVA	157-178		
			PVGLC_HSV11	3-84	467-486	PVGL2_IBVM	327-347	378-398	PVGL2_CVBF	1259-1280		
			PVGLC_HSV1K	3-84	467-486	PVGL2_IBVU2	310-330		PVGL2_CVBL9	1259-1280		
			PVGLC_HSVBC	476-494		PVGLB_EBV	732-752		PVGL2_CVBLY	1259-1280		
			PVGLG_CHAV	436-455		PVGLB_HCMVA	750-770		PVGL2_CVBM	1259-1280		
			PVGLG_RABVH	372-391		PVGLB_HCMVT	751-771		PVGL2_CVBQ	1259-1280		
			PVGLI_HSVEB	44-63		PVGLB_HSV23	79-99		PVGL2_CVBV	1259-1280		
			PVGLI_VZVD	278-297		PVGLB_HSV2H	79-99		PVGL2_CVM4	1317-1338		
			PVGLM_BUNGE	117-136		PVGLB_HSV29	65-85		PVGL2_CVMA5	1265-1286		
			PVGLM_PHV	152-171		PVGLB_HSV6U	72-92		PVGL2_CVMJH	1176-1197		
			PVGLM_PTPV	997-1016		PVGLB_HSVB2	279-299		PVGLB_HSV11	83-104		
			PVGLM_PUUMH	155-174		PVGLB_HSV8A	63-83		PVGLB_HSV1F	82-103		
			PVGLM_PUUMS	155-174		PVGLB_MCMVS	738-758		PVGLB_HSV1K	82-103		
			PVGLM_RVFV	830-849		PVGLF_PI3H4	283-303		PVGLB_HSV1P	83-104		
			PVGLM_RVFVZ	830-849		PVGLG_RABVE	454-474		PVGLB_MCMVS	136-156		
			PVGLM_UUK	656-674		PVGLG_RABVH	454-474		PVGLC_PRVIF	448-467		
			PVGLY_LYCVW	89-108		PVGLG_RABVP	454-474		PVGLF_CDVO	338-357		
			PVGNB_CPMV	1165-1184		PVGLG_RABV8	454-474		PVGLF_MEASE	224-245		
			PVM3_REOVD	521-540		PVGLG_RABVT	454-474		PVGLF_MEASI	227-246		
			PVME1_CVBM	171-190		PVGLH_MCMVS	670-690		PVGLF_MEASY	224-245		
			PVME1_CVH22	136-155		PVGLM_BUNL7	1325-1345		PVGLF_MUMPM	446-467		
			PVME1_CVPF5	174-193		PVGLM_BUN8H	1325-1345		PVGLF_MUMPR	446-467		
			PVME1_CVPPU	174-193		PVGLM_BUNYW	998-1016		PVGLF_MUMPS	446-467		
			PVME1_CVPRM	174-193		PVGLM_HANTB	998-1019		PVGLF_PHODV	305-326		
			PVME1_CVTKE	171-190		PVGLM_HANTH	1000-1020		PVGLF_PI1HC	456-477		
						PVGLM_HANTL	1001-1021		PVGLF_PI2H	450-471		
						PVGLM_HANTV	1001-1021		PVGLF_PI2HG	450-471		
						PVGLM_RVFVZ	1156-1176		PVGLF_PI2HT	450-471		
						PVGLM_SEOUR	1000-1020		PVGLF_PI3B	405-426	453-474	

						PVGLM_SEOUS	999-1019		PVGLF_PI3H4	453-474		
						PVGLM_UUK	925-945		PVGLF_RINDK	220-241		
						PVGLY_LYCVA	12-32		PVGLF_RINDL	220-241		
						PVGLY_LYCVW	12-32		PVGLF_SEND5	460-481		
						PVGLY_PIARV	12-32		PVGLF_SENDF	460-481		
						PVGNB_CPMV	141-161		PVGLF_SENDH	460-481		
						PVMAT_MUMPS	310-330		PVGLF_SENDJ	460-481		
						PVMAT_NDVA	309-329		PVGLF_SENDZ	460-481		
						PVMAT_NDVB	309-329		PVGLF_SV41	453-474		
						PVMAT_PI2HT	308-328		PVGLF_SV5	446-467		
						PVMAT_PI4HA	312-332		PVGLH_HCMVA	691-712		
						PVMAT_PI4HB	312-332		PVGLH_HCMVT	690-711		
						PVMAT_SV41	308-328		PVGLH_HSVE4	304-325		
						PVMAT_SV5	308-328		PVGLH_HSVEB	297-318		
						PVME1_IBV8	74-94		PVGLH_HSV3A	668-679		
						PVME1_IBVB	74-94		PVGLI_H8V2	2-23		
						PVME1_IBVB2	74-94		PVGLI_H9V23	2-23		
						PVME1_IBVK	74-94		PVGLM_BUNGE	197-218		
						PVMSA_HPBDB	201-221		PVGLM_BUNL7	190-211		
						PVMSA_HPBGS	209-229		PVGLM_BUNSH	190-211		
						PVMSA_HPBHE	293-313		PVGLM_BUNYW	193-214		
						PVMSA_WHV1	207-227		PVGLY_LASSG	237-258		
						PVMSA_WHV59	212-232		PVGLY_LASSJ	238-259		
						PVMSA_WHV7	212-232		PVGPS_EBV	67-88		
						PVMSA_WHV8	212-232		PVM01_VACCC	281-302		
						PVMSA_WHVBI	212-232		PVM01_VACCV	230-251		
						PVMSA_WHVW8	63-83		PVMAT_HRSVA	189-160		
									PVMAT_RINDK	200-221	239-260	
									PVMAT_TRTV	122-143		
									PVME1_CVHOC	64-85		
									PVMSA_HPBDB	201-222		
									PVMSA_HPBV0	70-91		
									PVMSA_HPBV2	244-265		
									PVMSA_HPBV4	244-265		
									PVMSA_HPBV9	244-265		
									PVMSA_HPBVA	233-254		
									PVMSA_HPBVD	70-91		
									PVMSA_HPBVI	233-254		
									PVMSA_HPBVJ	233-254		
									PVMSA_HPBVL	233-254		
									PVMSA_HPBVN	70-91		
									PVMSA_HPBVO	233-254		
									PVMSA_HPBVP	244-265		
									PVMSA_HPBVR	244-265		
									PVMSA_HPBVS	70-91		
									PVMSA_HPBVW	233-254		
									PVMSA_HPBVY	233-254		

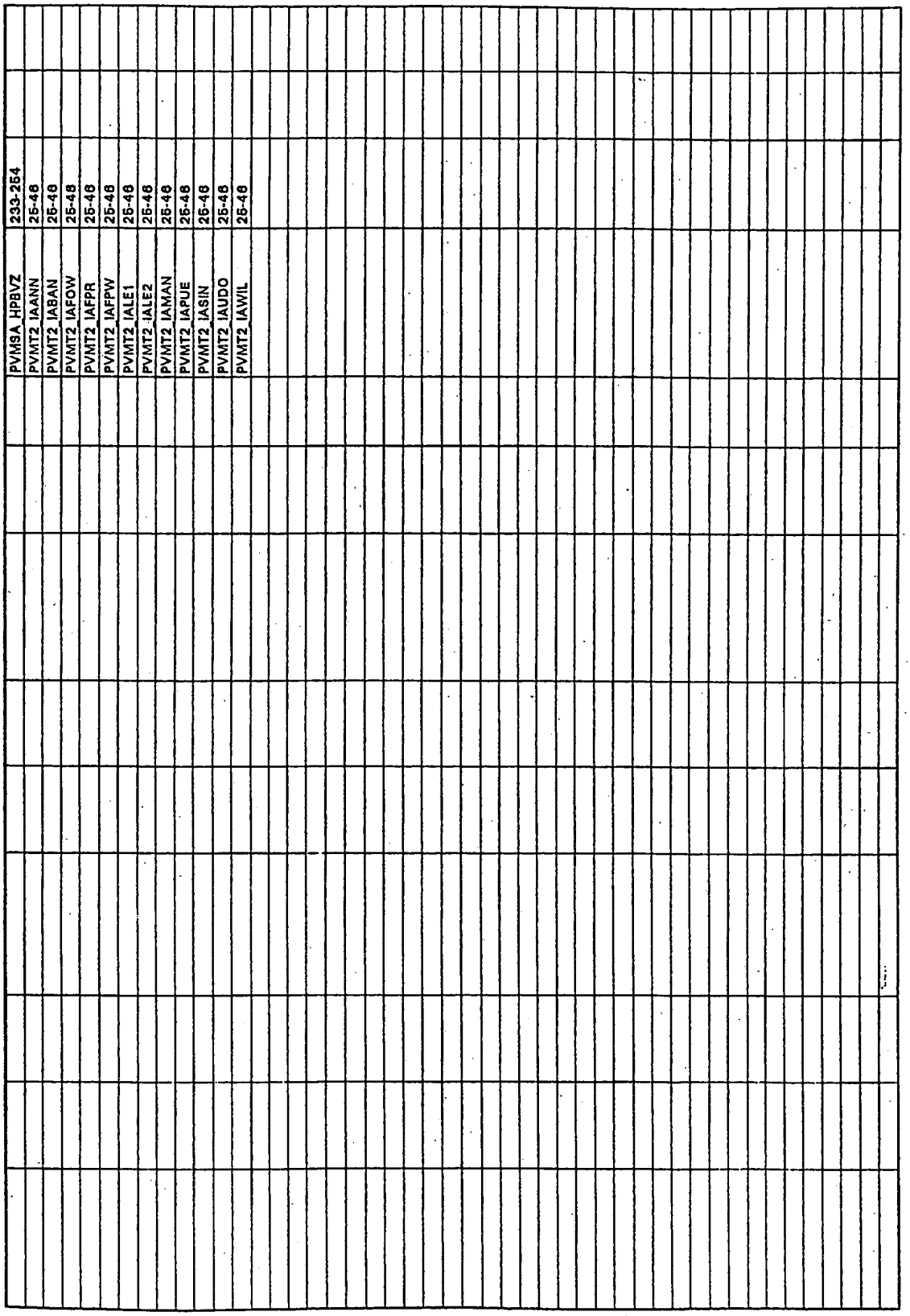
PVMSA_HPBVZ 233-254
PVMT2_IAANN 26-48
PVMT2_IABAN 26-48
PVMT2_IAFOW 26-48
PVMT2_IAFPR 26-48
PVMT2_IAFPW 26-48
PVMT2_IALE1 26-48
PVMT2_IALE2 26-48
PVMT2_IAMAN 26-48
PVMT2_IAPUE 26-48
PVMT2_IASIN 26-48
PVMT2_IAUDO 26-48
PVMT2_IAWIL 26-48

TABLE VIII

Search Results Summary for P7CTLZIP, P8CTLZIP, and P9CTLZIP Motifs

P7CTLZIP			P8CTLZIP			P8CTLZIP					
LIBRARY FILE			LIBRARY FILE			LIBRARY FILE					
PENV_BAEVM	202-224		PENV1_FRSFV	380-403		PENV_BLVAF	303-327				
PENV_HV1B1	498-520		PENV2_FRSFV	380-403		PENV_BLVAU	303-327				
PENV_HV1B8	493-515		PENV_BIV08	178-201		PENV_BLVAV	303-327				
PENV_HV1BN	494-516		PENV_BIV27	207-230		PENV_BLVB2	303-327				
PENV_HV1BR	503-525		PENV_FOAMV	864-887		PENV_BLVB5	303-327				
PENV_HV1EL	495-517		PENV_HV1Z3	176-198		PENV_BLVJ	303-327				
PENV_HV1H2	498-520		PENV_HV2BE	3-26	781-804	PENV_FIVPE	781-805				
PENV_HV1H3	498-520		PENV_HV2CA	750-773		PENV_FIVSD	779-803				
PENV_HV1J3	510-532		PENV_HV2D1	3-26	772-795	PENV_FIVT2	780-804				
PENV_HV1JR	490-512		PENV_HV2G1	772-795		PHEMA_CVBLY	391-415				
PENV_HV1KB	504-526		PENV_HV2NZ	777-800		PHEMA_CVBM	391-415				
PENV_HV1MA	500-522		PENV_JSRV	541-564		PHEMA_CVBQ	391-415				
PENV_HV1MF	498-518		PENV_SFV1	864-887		PHEMA_CVHOC	391-415				
PENV_HV1ND	488-510		PENV_SFV3L	861-884		PHEMA_INCCA	442-466				
PENV_HV1PV	498-520		PENV_SIVM1	803-826		PHEMA_INCEN	430-454				
PENV_HV1S1	488-511		PENV_SIVMK	802-825		PHEMA_INCGL	430-454				
PENV_HV1Z2	123-145	495-517	PENV_SIVML	801-824		PHEMA_INCHY	429-453				
PENV_HV1Z8	497-519		PENV_SIVS4	808-829		PHEMA_INCJH	443-467				
PENV_HV1Z8	505-527		PENV_SIVSP	810-833		PHEMA_INCKY	429-453				
PENV_HV1ZH	498-520		PHEMA_CDVO	200-223		PHEMA_INCMI	429-453				
PENV_JSRV	376-398		PHEMA_PI2H	65-88		PHEMA_INCNA	429-453				
PENV_MPMV	213-235		PHEMA_PI2HT	65-88		PHEMA_INCP1	430-454				
PENV_SRV1	213-235		PVF11_VACCC	161-184		PHEMA_INCP2	430-454				
PHEMA_IAAIC	37-59		PVF15_VACCC	25-48		PHEMA_INCP3	430-454				
PHEMA_IABAN	21-43		PVF15_VACCP	3-26		PHEMA_INCTA	430-454				
PHEMA_IADA3	37-59		PVG1L_AMEPV	313-336		PHEMA_INCYA	430-454				
PHEMA_IADH2	21-43		PVG28_HSVI1	491-514		PHEMA_MUMPM	101-125				
PHEMA_IADH3	21-43		PVG43_HSVI1	322-345		PHEMA_MUMPR	101-125				
PHEMA_IADH4	21-43		PVG52_HSVI1	229-252		PHEMA_MUMPS	101-125				
PHEMA_IADH5	21-43		PVG67_HSVI1	722-745		PHEMA_PI1HW	29-53				
PHEMA_IADH6	21-43		PVGL2_CVBF	10-33		PVENV_BEV	62-86				
PHEMA_IADH7	21-43		PVGL2_CVBL9	651-674		PVF05_VACCC	280-304				
PHEMA_IADM2	37-59		PVGL2_CVBLY	10-33		PVF05_VACCP	280-304				
PHEMA_IADMA	28-50		PVGL2_CVM4	1267-1290		PVF05_VACCV	281-305				
PHEMA_IADU3	37-59		PVGL2_CVMA5	1215-1238		PVF09_VACCC	176-200				
PHEMA_IAEN6	21-43		PVGL2_CVMJH	1126-1149		PVF09_VACCV	176-200				
PHEMA_IAEN7	37-59		PVGL2_CVPF8	1274-1297		PVG01_VZVD	58-82				
PHEMA_IAMAO	37-59		PVGL2_CVPPU	1272-1295		PVG10_HSVSA	355-379				
PHEMA_IAME1	37-59		PVGL2_CVPR8	1050-1073		PVG12_HSVSA	68-92				
PHEMA_IAME2	37-59		PVGL2_CVPRM	1050-1073		PVG19_HSVI1	88-112				
PHEMA_IAME6	21-43		PVGL2_FIPV	1277-1300		PVG28_HSVI1	173-197				
PHEMA_IANT6	37-59		PVGL2_IBV6	196-219		PVG43_HSVI1	108-133				
PHEMA_IAQU7	21-43		PVGL2_IBVB	195-218		PVG67_HSVI1	108-132	1005-1029			
PHEMA_IATKM	33-55		PVGL2_IBVD2	196-219		PVG72_HSVI1	720-744				
PHEMA_IAUDO	37-59		PVGL2_IBVD3	196-219		PVGF1_IBVB	3601-3625				

PHEMA_IAVI7	38-60		PVGL2_IBVK	195-218		PVGLB_HSVMD	589-613				
PHEMA_IAX31	37-59		PVGL2_IBVM	195-218		PVGLB_ILTV6	597-621				
PHEMA_IAZCO	37-59		PVGL2_IBVU1	178-201		PVGLB_ILTVS	607-631				
PHEMA_IAZH2	21-43		PVGL2_IBVU2	178-201		PVGLB_ILTVT	607-631				
PHEMA_IAZH3	21-43		PVGL2_IBVU3	178-201		PVGLE_HSV11	413-437				
PHEMA_IAZUK	37-59		PVGLB_HCMVA	535-558		PVGLE_VZVD	469-493				
PHEMA_PHODV	36-58		PVGLB_HCMVT	536-559		PVGLF_SV6	401-425				
PHEMA_PI2H	65-87		PVGLB_HSVSA	483-506		PVGLH_HCMVA	574-598				
PHEMA_PI2HT	65-87		PVGLB_MCMVS	566-589		PVGLH_HCMVT	573-597				
PVFP7_CAPVK	89-111		PVGLC_HSV11	467-490		PVGLH_HSV11	443-467	803-827			
PVFUS_VACC6	72-94		PVGLC_HSV1K	467-490		PVGLH_HSV1E	443-467	803-827			
PVG01_HSVI1	317-339		PVGLC_HSV2	435-458		PVGLM_BUNL7	31-55				
PVG03_VACCC	50-72		PVGLC_HSV23	438-459		PVGLM_BUNSH	31-55				
PVG03_VARV	50-72		PVGLM_BUNL7	1387-1410		PVGLM_HANTH	694-718				
PVG04_VACCC	11-33		PVGLM_BUNSH	1387-1410		PVGLM_RVFV	344-368				
PVG04_VARV	11-33		PVGLM_UUK	966-989		PVGLM_RVFVZ	344-368				
PVG19_HSVI1	88-110		PVGLY_JUNIN	12-35		PVGLM_UUK	561-585				
PVG28_HSVI1	173-195		PVGLY_LASSG	12-35		PVGNM_CPMV	311-335				
PVG29_HSVI1	20-42		PVGLY_LASSJ	12-35		PVGP2_EBV	657-681				
PVG46_HSVI1	134-156		PVGLY_LYCVA	12-35		PVGP3_EBV	854-878				
PVG48_HSVSA	71-93		PVGLY_LYCVW	12-35		PVM1_REOVD	280-304				
PVG58_HSVSA	266-288		PVGLY_MOPEI	12-35		PVM1_REOVL	280-304				
PVG59_HSVI1	267-289		PVGLY_TACV	12-35		PVM21_REOVD	168-192				
PVG5_SPV4	42-64		PVGLY_TACV6	12-35		PVM22_REOVD	168-192				
PVG60_HSVI1	53-75		PVGLY_TACV7	12-35		PVM2_REOVJ	168-192				
PVG65_HSVI1	1347-1369		PVGLY_TACVT	12-35		PVM2_REOVL	168-192				
PVG8_SPV1R	60-82		PVGNM_CPMV	741-764		PVMAT_MEASI	87-111				
PVGL2_IBV6	1056-1078		PVM1_REOVD	324-347	454-477	PVMAT_SSPVB	314-338				
PVGL2_IBVB	1055-1077		PVM1_REOVL	454-477		PVME1_CVBM	137-161				
PVGL2_IBVD2	1056-1078		PVMAT_MUMPS	227-250		PVME1_CVHOC	137-161				
PVGL2_IBVK	1055-1077		PVMSA_HPBDB	269-292		PVME1_CVTKE	137-161				
PVGL2_IBVM	1055-1077		PVMSA_HPBDC	268-291		PVME1_IBV6	74-98				
PVGLB_HSV6U	117-139		PVMSA_HPBDU	231-254		PVME1_IBVB	74-98				
PVGLB_HSVB2	745-767		PVMSA_HPBDW	269-292		PVME1_IBVB2	74-98				
PVGLC_HSVMB	399-421		PVMSA_HPBHE	236-259		PVME1_IBVK	74-98				
PVGLC_HSVMG	398-420					PVMSA_HPBGS	271-295				
PVGLC_HSVMM	399-421					PVMSA_WHV1	269-293				
PVGLF_BRSVA	265-287	482-504				PVMSA_WHV59	274-298				
PVGLF_BRSVC	484-506					PVMSA_WHV7	274-298				
PVGLF_BRSVR	484-506					PVMSA_WHV8	274-298				
PVGLF_HRSV1	484-506					PVMSA_WHV81	274-298				
PVGLF_HRSVA	484-506					PVMSA_WHVW8	125-149				
PVGLF_HRSVL	484-506										
PVGLF_HRSVR	484-506										
PVGLF_TRTV	452-474										
PVGLG_IHNV	77-99										
PVGLG_VHSV0	406-428										

PVGLH_HSVE4	814-836										
PVGLH_HSVEB	807-829										
PVGLI_HCMVA	158-180										
PVGLM_PTPV	743-765										
PVGLP_BEV	430-452	1546-1568									
PVGLY_LASSG	426-448										
PVGLY_LASSJ	427-449										
PVGLY_MOPEI	425-447										
PVGP2_EBV	657-679										
PVGP3_EBV	854-876										
PVM1_REOVD	414-436										
PVM1_REOVL	414-436										
PVM3_REOVD	304-326										
PVMAT_PI1HC	195-217										
PVMAT_PI2HT	132-154										
PVMAT_SENDF	195-217										
PVMAT_SENDH	195-217										
PVMAT_SENDZ	195-217										
PVMAT_SV41	132-154										
PVMEM_EBV	131-153										
PVMP_CERV	293-315										

TABLE IX

Search Results Summary for P12CTLZIP Motif

P12LZIPC												
LIBRARY FILE												
PENV1_FRSFV	380-407											
PENV2_FRSFV	380-407											
PENV_AVISU	98-117											
PENV_BAEVM	202-224											
PENV_BIV08	525-546											
PENV_BIV27	147-168	207-230	463-479	554-575								
PENV_BLVAF	303-327											
PENV_BLVAU	303-327											
PENV_BLVAV	303-327											
PENV_BLVB2	303-327											
PENV_BLVB5	303-327											
PENV_BLVJ	303-327											
PENV_FENV1	30-47	225-248	630-651									
PENV_FLVC8	38-55	624-645										
PENV_FLVGL	9-29	447-468	605-626									
PENV_FLVLB	467-488	613-646										
PENV_FLVSA	444-465	602-623										
PENV_FOAMV	153-174	255-275	300-325	481-498	710-727	884-887	924-951	957-978				
PENV_FSVGA	9-29	467-488	625-646									
PENV_FSVGB	447-468	605-626										
PENV_FSVGM	450-471	608-629										
PENV_FSVGT	467-488											
PENV_GALV	52-73	519-540										
PENV_HV1B1	498-520											
PENV_HV1B8	493-515											
PENV_HV1BN	494-516											
PENV_HV1BR	503-525											
PENV_HV1C4	428-448											
PENV_HV1EL	495-517											
PENV_HV1H2	498-520											
PENV_HV1H3	498-520											
PENV_HV1J3	510-532											
PENV_HV1JR	490-512											
PENV_HV1K8	504-526	552-579	752-788									
PENV_HV1MA	498-453	500-522										
PENV_HV1MF	495-518											
PENV_HV1ND	488-510											
PENV_HV1OY	123-140											
PENV_HV1PV	498-520											
PENV_HV1RH	445-460											
PENV_HV1S1	489-511	738-754										
PENV_HV1Z2	123-145	410-427	495-517									
PENV_HV1Z3	117-133	175-198										
PENV_HV1Z6	497-519											
PENV_HV1Z8	505-527											

PENV_HV1ZH	123-142	438-453	498-520									
PENV_HV2BE	3-26	750-775	781-804									
PENV_HV2CA	750-777											
PENV_HV2D1	3-26	741-766	772-795									
PENV_HV2D2	0-26											
PENV_HV2G1	741-766	772-795										
PENV_HV2NZ	742-767	777-800										
PENV_HV2RO	751-776											
PENV_HV2SB	743-768	778-804										
PENV_HV2ST	745-770											
PENV_JSRV	104-119	299-325	376-398	541-564								
PENV_MCFF	600-621											
PENV_MCFF3	601-622											
PENV_MLVAV	630-651											
PENV_MLVCB	625-646											
PENV_MLVF5	639-660											
PENV_MLVFF	639-660											
PENV_MLVFP	639-660											
PENV_MLVHO	626-647											
PENV_MLVKI	187-188											
PENV_MLVMO	629-650											
PENV_MLVRD	624-645											
PENV_MLVRK	624-645											
PENV_MMTVB	643-663											
PENV_MMTVG	643-663											
PENV_MPMV	213-235											
PENV_MSVFB	170-191											
PENV_OMVV5	76-100	658-683										
PENV_RMCFV	603-624											
PENV_RSVP	42-69	533-552										
PENV_SFV1	300-325	710-727	864-887	924-951	957-978							
PENV_SFV3L	157-178	304-329	707-724	861-884	921-948	954-975						
PENV_SIVA1	437-458											
PENV_SIVAG	442-463											
PENV_SIVAI	421-442											
PENV_SIVAT	435-456											
PENV_SIVGB	93-109											
PENV_SIVM1	766-793	803-826										
PENV_SIVM2	139-164	765-792	802-825									
PENV_SIVMK	139-164	764-791	801-824									
PENV_SIVML	769-789	806-829										
PENV_SIVS4	773-793	810-833										
PENV_SMSAV	42-63											
PENV_SRV1	213-235											
PHEMA_CDVO	36-53	200-223										
PHEMA_CVBLY	391-415											
PHEMA_CVBM	391-415											

PHEMA_CVBQ	391-415											
PHEMA_CVHOC	391-415											
PHEMA_CVMA5	402-423											
PHEMA_CVMS	403-418											
PHEMA_IAAIC	37-59	322-339										
PHEMA_IABAN	21-43	306-323										
PHEMA_IABUD	320-337											
PHEMA_IACKA	320-337											
PHEMA_IACKG	81-101	316-333										
PHEMA_IACKP	302-319											
PHEMA_IACKQ	302-319											
PHEMA_IACKS	319-336											
PHEMA_IACKV	230-246	315-332										
PHEMA_IADA1	320-337											
PHEMA_IADA2	319-336											
PHEMA_IADA3	37-59	322-339										
PHEMA_IADCZ	320-337											
PHEMA_IADE1	266-287											
PHEMA_IADH1	306-323											
PHEMA_IADH2	21-43	306-323										
PHEMA_IADH3	21-43	306-323										
PHEMA_IADH4	21-43	306-323										
PHEMA_IADH5	21-43											
PHEMA_IADH6	21-43	306-323										
PHEMA_IADH7	21-43	306-323										
PHEMA_IADM2	37-59	322-339										
PHEMA_IADMA	28-50	81-101										
PHEMA_IADNZ	320-337											
PHEMA_IADU3	37-59	322-339										
PHEMA_IAEN6	21-43	306-323										
PHEMA_IAEN7	37-59	322-339										
PHEMA_IAFPR	230-246	315-332										
PHEMA_IAGRE	320-337											
PHEMA_IAGU2	320-337											
PHEMA_IAGUA	319-336											
PHEMA_IAHAL	321-338											
PHEMA_IAHAR	230-246	315-332										
PHEMA_IAHC6	230-246	315-332										
PHEMA_IAHC7	230-246	315-332										
PHEMA_IAHCD	230-246	315-332										
PHEMA_IAHDE	230-246	315-332										
PHEMA_IAHFO	236-252	321-338										
PHEMA_IAHK6	321-338											
PHEMA_IAHK7	236-252	321-338										
PHEMA_IAHLE	230-246	315-332										
PHEMA_IAHLO	230-246	315-332										
PHEMA_IAHMI	236-252	321-338										

PHEMA_IAHNM	236-252	321-338										
PHEMA_IAHNN	315-332											
PHEMA_IAHPR	315-332											
PHEMA_IAHRO	236-252	321-338										
PHEMA_IAHSA	236-252	321-338										
PHEMA_IAHSP	230-246	315-332										
PHEMA_IAHSW	230-246	315-332										
PHEMA_IAHTE	236-252	321-338										
PHEMA_IAHTO	236-252	321-338										
PHEMA_IAHUR	236-252	321-338										
PHEMA_IAJAP	317-334											
PHEMA_IAMAA	197-223	319-336										
PHEMA_IAMAB	202-228	324-341										
PHEMA_IAMAO	37-59	322-339										
PHEMA_IAME1	37-59	322-339										
PHEMA_IAME2	37-59	322-339										
PHEMA_IAME6	21-43											
PHEMA_IAMIN	85-101	231-247	316-333									
PHEMA_IANT6	37-59	322-339										
PHEMA_IAPIL	320-337											
PHEMA_IAQU7	21-43	306-323										
PHEMA_IARUD	320-337											
PHEMA_IASE2	320-337											
PHEMA_IASH2	321-338											
PHEMA_IASTA	230-246	315-332										
PHEMA_IATAI	33-55	320-337										
PHEMA_IATKI	233-249											
PHEMA_IATKR	230-246											
PHEMA_IATKW	229-245.											
PHEMA_IAUDO	37-59	322-339	380-397									
PHEMA_IAVI7	38-60	323-340										
PHEMA_IAX31	37-59											
PHEMA_IAZCO	37-59	322-339										
PHEMA_IAZH2	21-43	306-323										
PHEMA_IAZH3	21-43	306-323										
PHEMA_IAZUK	37-59	322-339										
PHEMA_INBAA	115-131	295-310										
PHEMA_INBBE	123-139	303-318										
PHEMA_INBBO	116-132	293-308										
PHEMA_INBEN	123-139	301-316										
PHEMA_INBFU	108-124	286-301										
PHEMA_INBGL	119-135	296-311										
PHEMA_INBHK	116-132	293-308										
PHEMA_INBIB	108-124	288-303										
PHEMA_INBID	120-136	299-314										
PHEMA_INBLE	123-139	302-317										
PHEMA_INBMD	113-129	292-307										

PHEMA_INBME	116-132	298-311										
PHEMA_INBNA	108-124	288-303										
PHEMA_INBOR	123-139	301-316										
PHEMA_INBSI	123-139	301-316										
PHEMA_INBSJ	119-135	298-313										
PHEMA_INBUS	116-132	294-309										
PHEMA_INBVI	116-132	296-311										
PHEMA_INBVK	123-139	303-318										
PHEMA_INBYB	108-124	286-301										
PHEMA_INCCA	442-466											
PHEMA_INCEN	430-454											
PHEMA_INCGL	430-454											
PHEMA_INCHY	429-453											
PHEMA_INCJH	443-467											
PHEMA_INCKY	429-453											
PHEMA_INCMI	429-453											
PHEMA_INCNA	429-453											
PHEMA_INCP1	430-454											
PHEMA_INCP2	430-454											
PHEMA_INCP3	430-454											
PHEMA_INCTA	430-454											
PHEMA_INCYA	430-454											
PHEMA_MUMPM	133-148	225-246	367-394	397-417								
PHEMA_MUMPR	101-125	133-148	225-246	397-417								
PHEMA_MUMPS	101-125	133-148	225-246	367-394	397-417							
PHEMA_NDVA	93-110											
PHEMA_NDVB	93-110											
PHEMA_NDVD	93-110											
PHEMA_NDVH	93-110											
PHEMA_NDVI	93-110											
PHEMA_NDVM	93-110											
PHEMA_NDVQ	93-110											
PHEMA_NDVTG	93-110											
PHEMA_NDVU	93-110											
PHEMA_PHODV	36-58	213-234	493-513									
PHEMA_PI1HW	29-53	322-342	346-360	486-503								
PHEMA_PI2H	13-40	66-88	118-136									
PHEMA_PI2HT	13-40	66-88	118-136									
PHEMA_PI3B	111-128	272-299	324-340									
PHEMA_PI3H4	111-128	272-299	324-340									
PHEMA_PI3HA	111-128	272-299	324-340									
PHEMA_PI3HT	111-128	272-299	324-340									
PHEMA_PI3HU	111-128	272-299	324-340									
PHEMA_PI3HV	111-128	272-299	324-340									
PHEMA_PI3HW	111-128	272-299	324-340									
PHEMA_PI3HX	111-128	272-299	324-340									
PHEMA_PI4HA	60-87											

PHEMA_RINDK	368-383											
PHEMA_RINDL	4-30											
PHEMA_SEND5	322-342											
PHEMA_SENDF	322-342											
PHEMA_SENDH	322-342											
PHEMA_SENDJ	322-342											
PHEMA_SENDZ	322-342											
PHEMA_SV41	56-73	86-102	107-132									
PHEMA_SV5	7-26	84-101	379-400									
PHEMA_SV5CM	7-26	84-101	379-400.									
PHEMA_SV5CP	7-26	84-101	379-400.									
PHEMA_SV5LN	7-26	84-101	379-400.									
PHEMA_VACCC	173-192											
PHEMA_VACCI	173-192											
PHEMA_VACCT	173-192											
PHEMA_VACCV	173-192											
PVENV_BEV	62-86	87-114										
PVENV_DHVI1	42-57	484-511										
PVENV_EAV	25-41											
PVENV_LELV	27-47	148-168										
PVENV_MCV1	61-80											
PVENV_MCV2	61-80	306-333										
PVENV_THOGV	198-221	358-383	473-491									
PVF05_VACCC	280-305											
PVF05_VACCP	280-305											
PVF05_VACCV	280-305											
PVF09_VACCC	178-200											
PVF09_VACCV	178-200											
PVF11_VACCC	161-184											
PVF15_VACCC	25-48											
PVF15_VACCP	3-26											
PVFP1_FOWPV	297-323											
PVFP2_FOWPV	88-104											
PVFP7_CAPVK	89-111											
PVFP7_FOWPV	65-90											
PVFP8_CAPVK	51-76											
PVFU8_ORFNZ	29-48											
PVFU8_VACC8	72-94											
PVG01_HSVEB	169-195											
PVG01_HSVI1	210-225	317-339	589-616									
PVG01_VACCC	298-318	376-395										
PVG01_VACCV	237-257	315-334										
PVG01_VARV	298-318	376-395										
PVG01_VZVD	58-82											
PVG03_VACCC	50-72											
PVG03_VARV	50-72											
PVG04_VACCC	11-33											

PVG04_VARV	11-33											
PVG08_VACCC	31-51											
PVG06_VARV	31-51											
PVG08_HSVI1	134-149	159-185										
PVG10_HSVI1	35-54											
PVG10_HSV8A	109-124	355-379										
PVG11_HSVI1	103-122	150-176										
PVG12_HSVI1	151-178	270-286										
PVG12_HSVSA	68-92											
PVG15_HSVEB	184-209											
PVG19_HSVI1	88-112											
PVG1L_AMEPV	313-336											
PVG1_SPV1R	76-92	659-678										
PVG22_HSVI1	300-327											
PVG23_HSVI1	314-336											
PVG27_HSVI1	158-184											
PVG27_HSVSA	209-226											
PVG28_HSVI1	173-197	491-518										
PVG28_HSVSA	14-40											
PVG29_HSVI1	20-42											
PVG30_HSVI1	166-191											
PVG32_VZVD	90-109											
PVG36_HSVSA	108-123	344-362										
PVG37_HSVI1	264-289											
PVG39_HSVI1	648-675	970-990	1038-1065									
PVG40_HSVI1	14-32											
PVG41_HSVI1	11-38	62-81	244-260									
PVG43_HSVI1	109-133	157-178	322-345	521-538								
PVG46_HSVI1	134-156	580-607	937-963	1244-1270								
PVG48_HSV8A	71-93											
PVG50_HSVI1	5-30	58-83										
PVG50_HSV8A	63-81	95-117	206-233									
PVG51_HSVI1	28-49	84-102										
PVG52_HSVI1	229-252											
PVG55_HSVI1	22-37	143-159	288-309									
PVG55_HSV8A	85-106											
PVG56_HSVI1	1155-1176											
PVG58_HSV6A	130-146	266-288	293-319	330-346								
PVG59_HSVI1	142-161	267-289										
PVG5_SPV4	42-64											
PVG60_HSVI1	30-51	53-75										
PVG61_HSVI1	76-102	117-136										
PVG63_HSVI1	238-259	336-363										
PVG64_HSVI1	420-445											
PVG65_HSVI1	117-137	155-173	362-378	518-533	1147-1174	1347-1369						
PVG67_HSVI1	108-132	171-188	318-344	722-745	1005-1029	1072-1091	1315-1341					
PVG6_SPV1R	60-82											

PVG70_HSVI1	184-209											
PVG71_HSVSA	89-105											
PVG72_HSVI1	445-471	535-561	720-744	1252-1269								
PVG74_HSVSA	124-151											
PVG9_SPV1R	57-72											
PVGF1_IBVB	1587-1606	1856-1877	2108-2127	2210-2226	2788-2806	2973-2999	3073-3090	3374-3399	3601-3625			
PVGH3_HCMVA	157-178											
PVGL2_CVBF	10-33	123-139	174-190	264-279	991-1017	1259-1280						
PVGL2_CVBL9	123-139	174-190	264-279	651-674	991-1017	1259-1280						
PVGL2_CVBLY	10-33	123-139	174-190	264-279	991-1017	1259-1280						
PVGL2_CVBM	123-139	174-190	264-279	991-1017	1259-1280							
PVGL2_CVBQ	31-47	123-139	174-190	991-1017	1259-1280							
PVGL2_CVBV	123-139	174-190	264-279	991-1017	1259-1280							
PVGL2_CVH22	768-794.	1053-1071	1115-1134									
PVGL2_CVM4	95-111	999-1025	1207-1290	1317-1338								
PVGL2_CVMA5	95-111	947-973	1215-1238	1265-1286								
PVGL2_CVMJH	95-111	858-884	1126-1149	1176-1197								
PVGL2_CVPFS	64-83	442-457	800-816	1038-1064	1274-1297							
PVGL2_CVPPU	64-83	440-455	504-519	798-814	1036-1062	1272-1295						
PVGL2_CVPR8	218-233	576-592	814-840	1050-1073								
PVGL2_CVPRM	218-233	576-592	814-840	1050-1073								
PVGL2_FIPV	803-819	1041-1067	1277-1300									
PVGL2_IBV6	196-219	588-607	771-797	1056-1081	1094-1111							
PVGL2_IBVB	195-218	587-606	770-796	1055-1080								
PVGL2_IBVD2	196-219	588-607	771-797	1056-1081								
PVGL2_IBVD3	196-219											
PVGL2_IBVK	195-218	587-606	770-796	1055-1080								
PVGL2_IBVM	195-218	378-398	587-606	770-796	1055-1080							
PVGL2_IBVU1	178-201											
PVGL2_IBVU2	178-201											
PVGL2_IBVU3	178-201											
PVGL8_EBV	732-752											
PVGL8_HCMVA	535-558	708-732	750-777									
PVGL8_HCMVT	536-559	707-733	751-778									
PVGL8_HSV11	83-104											
PVGL8_HSV1F	82-103											
PVGL8_HSV1K	82-103											
PVGL8_HSV1P	83-104											
PVGL8_HSV23	78-99											
PVGL8_HSV2H	78-99											
PVGL8_HSV2S	65-85											
PVGL8_HSV8U	72-92	117-144										
PVGL8_HSVB1	560-578	689-707										
PVGL8_HSVB2	279-298	745-767										
PVGL8_HSVBC	692-710											
PVGL8_HSVE1	736-753											
PVGL8_HSVE4	675-692											

PVGLB_HSVEA	736-753											
PVGLB_HSVEB	736-753											
PVGLB_HSVEL	736-753											
PVGLB_HSVMD	589-613											
PVGLB_HSVSA	483-506	584-602	701-718									
PVGLB_ILTVB	256-275	597-621	740-758									
PVGLB_ILTVS	266-285	607-631	750-768									
PVGLB_ILTVT	266-285	607-631	750-768									
PVGLB_MCMVS	135-156	586-589	738-755									
PVGLB_PRVIF	203-218											
PVGLB_VZVD	522-538											
PVGLC_HSV11	467-493											
PVGLC_HSV1K	3-22	467-493										
PVGLC_HSV2	436-458											
PVGLC_HSV23	436-459											
PVGLC_HSVBC	476-494											
PVGLC_HSVE4	444-459											
PVGLC_HSVEB	427-442											
PVGLC_HSVMB	399-421											
PVGLC_HSVMG	398-420											
PVGLC_HSVMM	399-421											
PVGLC_PRVIF	180-197	446-472										
PVGLC_VZVD	431-449											
PVGLC_VZVS	431-449											
PVGLD_HSV11	79-94											
PVGLD_HSV2	79-94											
PVGLE_HSV11	104-129	413-437										
PVGLE_VZVD	469-493											
PVGLF_BRSVA	205-221	265-287	482-504									
PVGLF_BRSVC	205-221	265-287	484-506									
PVGLF_BRSVR	205-221	265-287	484-506									
PVGLF_CDVO	336-361	398-414	582-599									
PVGLF_HRSV1	205-221	265-287	484-506									
PVGLF_HRSVA	205-221	265-287	484-506									
PVGLF_HRSVL	205-221	265-287	484-506									
PVGLF_HRSVR	205-221	265-287	484-506									
PVGLF_MEASE	224-245	286-302	451-477									
PVGLF_MEASI	227-248	289-305	454-480									
PVGLF_MEASY	224-245	286-302	451-477									
PVGLF_MUMPM	276-292	446-467										
PVGLF_MUMPR	276-292	446-467										
PVGLF_MUMPS	5-20	276-292	446-467									
PVGLF_NDVA	273-289											
PVGLF_NDVB	273-289											
PVGLF_NDVM	273-289											
PVGLF_NDVT	273-289											
PVGLF_NDVTG	273-289											

PVGLF_NDVU	273-289											
PVGLF_PHODV	288-285	305-326	387-383	531-558								
PVGLF_PI1HC	456-477											
PVGLF_PI2H	460-471											
PVGLF_PI2HG	460-471											
PVGLF_PI2HT	450-471											
PVGLF_PI3B	283-310	405-426	453-474									
PVGLF_PI3H4	2-20	283-310	453-474									
PVGLF_RINDK	220-241	282-298	447-473									
PVGLF_RINDL	220-241	282-298	447-473									
PVGLF_SEND5	460-481											
PVGLF_SENDF	460-481											
PVGLF_SENDH	460-481											
PVGLF_SENDJ	460-481											
PVGLF_SENDZ	460-481											
PVGLF_SV41	453-474											
PVGLF_SV5	401-425	446-467										
PVGLF_TRTV	175-191	452-474										
PVGLG_IHNV	77-99											
PVGLG_RABVE	454-474											
PVGLG_RABVH	372-391	454-474										
PVGLG_RABVP	454-474											
PVGLG_RABVS	454-474											
PVGLG_RABVT	454-474											
PVGLG_VHSV0	408-428											
PVGLH_HCMVA	211-237	385-382	574-598	691-712								
PVGLH_HCMVT	210-238	384-381	573-597	690-711								
PVGLH_HSV11	245-262	443-467	803-827									
PVGLH_HSV1E	245-262	443-467	803-827									
PVGLH_HSV8G	314-332											
PVGLH_HSVE4	304-325	814-839										
PVGLH_HSVEB	297-318	807-832										
PVGLH_HSVSA	454-479	658-679										
PVGLH_MCMVS	670-690											
PVGLI_HCMVA	158-180											
PVGLI_HSV11	43-60											
PVGLI_HSVEB	44-63											
PVGLI_VZVD	278-297											
PVGLM_BUNGE	117-136	197-222										
PVGLM_BUNL7	31-55	81-98	190-211	1325-1345	1387-1410							
PVGLM_BUNSH	31-55	81-98	190-211	1325-1345	1387-1410							
PVGLM_BUNYW	193-218	1379-1404										
PVGLM_HANTB	355-371	692-717	900-915	999-1019								
PVGLM_HANTH	499-515	694-718	1000-1020									
PVGLM_HANTL	499-515	694-718	1001-1021									
PVGLM_HANTV	499-515	694-718	1001-1021									
PVGLM_PHV	162-171											

PVGLM_PTPV	743-765	997-1016	1276-1302									
PVGLM_PUUMH	155-174	509-525	712-729									
PVGLM_PUUMS	155-174	509-525	712-729	1092-1117								
PVGLM_RVFV	53-80	344-368	830-856									
PVGLM_RVFVZ	53-80	344-368	830-856	1156-1176								
PVGLM_SEOUR	355-371	693-718	901-916	1000-1020								
PVGLM_SEOUS	356-371	692-717	900-915	999-1019								
PVGLM_UUK	561-585	656-674	826-842	926-952	966-989							
PVGLP_BEV	430-452	869-885	1099-1124	1546-1568								
PVGLX_PRVRI	149-176											
PVGLY_JUNIN	12-38											
PVGLY_LASSG	12-38	237-258	426-448									
PVGLY_LASSJ	12-38	238-259	427-449									
PVGLY_LYCVA	12-38											
PVGLY_LYCVW	12-38	89-108										
PVGLY_MOPEI	12-38	425-447										
PVGLY_PIARV	12-38	441-466										
PVGLY_TACV	12-38											
PVGLY_TACV6	12-38											
PVGLY_TACV7	12-38											
PVGLY_TACVT	12-38											
PVGNB_CPMV	141-161	589-594	757-783	1110-1135	1165-1184							
PVGNM_BPMV	678-696											
PVGNM_CPMV	311-335	741-764	1021-1037									
PVGP2_EBV	657-681											
PVGP3_EBV	854-878											
PVGP8_EBV	67-88											
PVM01_VACCC	134-159	177-195	281-302									
PVM01_VACCV	83-108	126-144	230-251									
PVM1_REOVD	141-168	227-245	280-304	324-347	414-438	454-477						
PVM1_REOVL	141-168	227-245	280-304	414-438	454-477							
PVM21_REOVD	168-192											
PVM22_REOVD	168-192											
PVM2_REOVJ	168-192											
PVM2_REOVL	168-192											
PVM3_REOVD	304-328	521-540										
PVMAT_BRSVA	37-62											
PVMAT_CDVO	148-165	283-309										
PVMAT_HRSVA	44-62	139-160										
PVMAT_LPMV	311-338											
PVMAT_MEASE	283-309											
PVMAT_MEASH	283-309											
PVMAT_MEASI	87-111											
PVMAT_MEASU	283-309											
PVMAT_MUMPS	191-207	227-250	310-330									
PVMAT_NDVA	135-151	190-208	309-329									
PVMAT_NDVB	135-151	190-208	309-329									

PVMAT_PI1HC	195-217											
PVMAT_PI2HT	132-154	189-205	308-328									
PVMAT_PI4HA	312-332											
PVMAT_PI4HB	312-332											
PVMAT_RINDK	200-221	239-260	283-309									
PVMAT_SENDF	195-217											
PVMAT_SENDH	195-217											
PVMAT_SENDZ	195-217											
PVMAT_S8PVB	283-309	314-338										
PVMAT_SV41	132-154	189-205	308-328									
PVMAT_SV5	98-114	132-148	308-336									
PVMAT_SVCV	141-167											
PVMAT_TRTV	122-143											
PVME1_CVBM	9-36	137-161	171-190									
PVME1_CVH22	136-156											
PVME1_CVHOC	9-36	64-86	137-161									
PVME1_CVMA5	10-37											
PVME1_CVMJH	10-37											
PVME1_CVPFS	174-193											
PVME1_CVPPU	174-193											
PVME1_CVPRM	174-193											
PVME1_CVTKE	9-36	137-161	171-190									
PVME1_IBV6	74-98											
PVME1_IBVB	74-101											
PVME1_IBVB2	74-101											
PVME1_IBVK	74-98											
PVMEM_EBV	131-157	178-203										
PVMP_CAMVC	118-134	147-164	183-201									
PVMP_CAMVD	118-134	147-164	183-201									
PVMP_CAMVE	118-134	147-164	183-201									
PVMP_CAMVN	118-134	147-164	183-201									
PVMP_CAMVS	118-134	147-164	183-201									
PVMP_CAMVW	118-134	147-164	183-201									
PVMP_CERV	293-318											
PVMP_FMVD	115-131	180-198										
PVMP_SOCMV	122-147	273-299										
PVMSA_HPBDB	201-228	269-295										
PVMSA_HPBDC	194-221	268-294										
PVMSA_HPBDU	157-184	231-257										
PVMSA_HPBDW	194-221	269-295										
PVMSA_HPBGS	209-236	271-296	380-395									
PVMSA_HPBHE	236-262	293-320										
PVMSA_HPBV0	70-98											
PVMSA_HPBV2	185-202	244-270										
PVMSA_HPBV4	185-202	244-270										
PVMSA_HPBV9	244-270											
PVMSA_HPBVA	174-191	233-259										

PVMSA_HPBVD	11-28	70-86										
PVMSA_HPBVI	233-259											
PVMSA_HPBVJ	174-191	233-259										
PVMSA_HPBVL	174-191	233-259										
PVMSA_HPBVN	11-28	70-86										
PVMSA_HPBVO	174-191	233-259										
PVMSA_HPBVP	185-202	244-270										
PVMSA_HPBVR	185-202	244-270										
PVMSA_HPBVS	11-28	70-86										
PVMSA_HPBVW	174-191	233-259										
PVMSA_HPBVY	174-191	233-259										
PVMSA_HPBVZ	174-191	233-259										
PVMSA_WHV1	207-234	269-293	378-393									
PVMSA_WHV59	212-239	274-298	383-398									
PVMSA_WHV7	212-239	274-298	383-398									
PVMSA_WHV8	212-239	274-298	383-398									
PVMSA_WHV8I	212-239	274-298	383-398									
PVMSA_WHVW6	125-149	234-249										
PVMT2_IAANN	25-46											
PVMT2_IABAN	25-46											
PVMT2_IAFOW	25-46											
PVMT2_IAFPR	25-46											
PVMT2_IAFPW	25-46											
PVMT2_IALE1	25-46											
PVMT2_IALE2	25-46											
PVMT2_IAMAN	25-46											
PVMT2_IAPUE	25-46											
PVMT2_IASIN	25-46											
PVMT2_IAUDO	25-46											
PVMT2_IAWIL	25-46											
PVMT9_MYXVL	226-241											

TABLE X

Search Results Summary for P23CTLZIP Motif

P23LZIPC							
LIBRARY FILE							
PENV_AVI9U	88-136						
PENV_BAEVM	202-240	526-554					
PENV_BIV08	434-472	526-553	828-859				
PENV_BIV27	554-582	867-888					
PENV_CAEVG	44-78						
PENV_EIAV1	795-828						
PENV_EIAV2	795-828						
PENV_EIAV3	795-828						
PENV_EIAV5	795-828						
PENV_EIAV9	795-828						
PENV_EIAVC	795-828						
PENV_EIAVW	795-828						
PENV_EIAVY	795-828						
PENV_FIVPE	128-168						
PENV_FIVT2	46-74						
PENV_FLVGL	447-475						
PENV_FLVLB	407-485						
PENV_FLV8A	444-472						
PENV_FOAMV	44-78	481-519	552-584				
PENV_FR9FB	315-350						
PENV_F8VGA	407-495						
PENV_F8VGB	447-475						
PENV_F9V8M	460-478						
PENV_F8V8T	467-495						
PENV_GALV	519-554						
PENV_HV1A2	728-762						
PENV_HV1B1	730-763						
PENV_HV1BB	726-768						
PENV_HV1BN	743-781						
PENV_HV1BR	735-768						
PENV_HV1C4	742-775						
PENV_HV1EL	264-286	727-780					
PENV_HV1H2	730-763						
PENV_HV1H3	730-763						
PENV_HV1J3	741-774						
PENV_HV1JR	722-765						
PENV_HV1KB	662-688	762-790					
PENV_HV1MA	258-288	733-768					
PENV_HV1MF	728-761						
PENV_HV1MN	392-430	731-784					
PENV_HV1ND	248-278						
PENV_HV1OY	729-762						
PENV_HV1PV	730-763						
PENV_HV1RH	739-772						
PENV_HV1SC	730-763						

PENV_HV1W1	730-783						
PENV_HV1W2	721-764						
PENV_HV1Z2	264-286	727-760					
PENV_HV1Z3	260-281						
PENV_HV1Z8	265-288	728-762					
PENV_HV1Z8	265-288						
PENV_HV28E	781-811						
PENV_HV2D1	772-802						
PENV_HV2G1	772-802						
PENV_HV2N2	777-814						
PENV_HV2S8	743-776						
PENV_J8RV	288-332	484-516					
PENV_MMTVB	436-472						
PENV_MMTVG	436-472						
PENV_RSVP	633-670						
PENV_8FV1	44-78	492-530					
PENV_8FV3L	48-82	550-588					
PENV_8IVCZ	746-778						
PENV_8IVG8	247-277	353-386					
PENV_8IVM1	788-800						
PENV_8IVMK	786-798						
PENV_8IVML	611-645	784-798					
PENV_8IV84	458-488						
PENV_8IV8P	462-480	810-840					
PHEMA_CDVO	200-234						
PHEMA_IABUD	23-55						
PHEMA_IACKA	23-55						
PHEMA_IACKV	617-647						
PHEMA_IADA1	23-55						
PHEMA_IADC2	23-55						
PHEMA_IADH5	283-323						
PHEMA_IADNZ	23-55						
PHEMA_IAFPR	16-51						
PHEMA_IAGRE	23-55						
PHEMA_IAMAA	22-54						
PHEMA_IAMA8	27-59						
PHEMA_IARUD	23-55						
PHEMA_IASE2	23-55						
PHEMA_IA8TA	617-647						
PHEMA_MUMPM	19-52	101-132					
PHEMA_MUMPR	19-52	101-132					
PHEMA_MUMP8	19-52	101-132					
PHEMA_NDVA	60-88						
PHEMA_NDVB	60-88						
PHEMA_NDVD	60-88						
PHEMA_NDVH	60-88						
PHEMA_NDVI	60-88						

PHEMA_NDVM	60-88				
PHEMA_NDVQ	60-88				
PHEMA_NDVTQ	60-88				
PHEMA_NDVU	60-88				
PHEMA_PI1HW	28-60	188-233			
PHEMA_PI2H	13-48	334-389			
PHEMA_PI2HT	13-48	334-389			
PHEMA_PI3B	184-231				
PHEMA_PI3H4	184-231				
PHEMA_PI3HA	184-231				
PHEMA_PI3HT	184-231				
PHEMA_PI3HU	184-231				
PHEMA_PI3HV	184-231				
PHEMA_PI3HW	184-231				
PHEMA_PI3HX	184-231				
PHEMA_PI4HA	245-280	338-376			
PHEMA_RACVI	255-293				
PHEMA_RINDL	282-313				
PHEMA_SEND6	18-54	188-233			
PHEMA_SENDF	18-54	188-233			
PHEMA_SENDH	18-54	188-233			
PHEMA_SENDJ	18-54	188-233			
PHEMA_SEND2	23-64	188-233			
PHEMA_SV41	56-84	330-385			
PHEMA_SV5	7-35				
PHEMA_SV5CM	7-41				
PHEMA_SV5CP	7-41				
PHEMA_SV5LN	7-35				
PHEMA_VACCC	258-284				
PHEMA_VACCI	258-284				
PHEMA_VACCT	258-284				
PHEMA_VACCV	258-284				
PVENV_BEV	18-61	87-117			
PVENV_DHVI1	297-335				
PVENV_MCV1	203-238				
PVENV_MCV2	203-238				
PVENV_VACCC	208-241				
PVENV_VACCI	208-241				
PVENV_VACCP	208-241				
PVENV_VACCV	208-241				
PVF03_VACCC	2-40	61-83			
PVF03_VACCV	2-40	61-83			
PVFP1_FOWPV	297-330				
PVFP4_FOWPV	237-267				
PVFP7_CAPVK	89-118				
PVFU8_VACCC	28-61				
PVFU8_VACCV	28-61				

PVG01_H3V11	317-346					
PVG02_H8VEB	163-198					
PVG02_VACCV	82-120					
PVG02_VARV	82-120					
PVG03_H3V11	108-138					
PVG08_H5V11	54-83					
PVG06_VACCC	99-138					
PVG06_VARV	99-138					
PVG07_VACCC	113-145					
PVG07_VARV	113-145					
PVG09_VACCC	303-338					
PVG09_VACCV	288-301					
PVG09_VARV	303-338					
PVG11_H6V11	150-183					
PVG12_H3V11	208-243					
PVG12_H6V6A	68-108					
PVG1_SPV1R	254-292	303-337	414-462			
PVG22_H6V11	300-337	647-678				
PVG23_H3V11	70-108					
PVG26_H6V11	84-125					
PVG27_H3V3A	38-74					
PVG28_H8V11	491-521					
PVG28_H3V8A	7-40					
PVG2R_AMEPV	180-217					
PVG2_SPV4	209-244					
PVG35_H6V11	15-48	180-228				
PVG36_H3V3A	151-185					
PVG38_H6V11	643-677	648-682				
PVG40_H3V3A	187-218					
PVG41_H6V11	11-45	202-233				
PVG42_H3V11	91-126					
PVG43_H6V11	108-140	157-186				
PVG46_H3V11	888-925					
PVG48_H6V8A	328-367					
PVG50_H3V8A	113-141					
PVG51_H6V11	28-64	84-120				
PVG52_H6V11	98-134					
PVG55_H6V11	100-129					
PVG56_H8V11	631-667	1081-1128				
PVG58_H6V11	342-376	480-508				
PVG58_H3V3A	26-60	196-233				
PVG59_H3V11	82-118					
PVG61_H3V11	78-109					
PVG64_H6V11	56-89	383-401	420-462			
PVG65_H3V11	801-838	1290-1328				
PVG67_H6V11	150-188	1150-1185				
PVG8_SPV1R	60-89					

PVG71_H8V9A	128-158					
PVG72_H8VI1	446-478	720-761	1158-1189	1262-1286		
PVG75_H8VI1	283-291	387-422				
PVG78_H8VI1	187-221					
PVG7_8PV1R	18-46					
PVGF1_IBVB	1718-1747	1858-1891	2108-2148	3601-3633		
PVGH3_HCMVA	80-115	157-185				
PVGL2_CVBF	1259-1284					
PVGL2_CVBL9	661-681	1258-1284				
PVGL2_CVBLY		1258-1284				
PVGL2_CVBM		1258-1284				
PVGL2_CVBQ		1258-1284				
PVGL2_CVBV		1258-1284				
PVGL2_CVH22	1053-1088					
PVGL2_CVM4	1287-1304					
PVGL2_CVMA5	1215-1252					
PVGL2_CVMJH	1128-1163					
PVGL2_CVPF6	632-685	738-784	1328-1383			
PVGL2_CVPPU	630-663	734-782	1328-1361			
PVGL2_CVPR8	512-540	1104-1139				
PVGL2_CVPRM	408-441	1104-1139				
PVGL2_FIPV	635-688	738-787	1331-1366			
PVGL2_IBVB	153-188					
PVGLB_HCMVA	116-147	706-743				
PVGLB_HCMVT	116-147	707-744				
PVGLB_H8VBU	72-110					
PVGLB_H8VB1	254-288					
PVGLB_H8VB2	284-288	745-774				
PVGLB_H8VBC	253-287					
PVGLB_ILTV8	442-472					
PVGLB_ILTVS	452-482					
PVGLB_ILTVT	452-482					
PVGLB_MCMV3	136-163	738-778				
PVGLC_H8V11	467-500					
PVGLC_H8V1K	467-500					
PVGLC_H8V2	436-465					
PVGLC_H8V23	438-466					
PVGLC_H8VBC	478-507					
PVGLC_VZVD	351-388	513-548				
PVGLC_VZVS	351-388	513-548				
PVGLD_H8VEA	340-370					
PVGLD_H8VEB	41-70	390-420				
PVGLD_H8VEK	41-70	390-420				
PVGLE_H8VE4	86-126					
PVGLE_H8VEB	63-100	390-420				
PVGLE_H8VEL	63-100	392-422				
PVGLE_PRVRI	332-369					

PVGLF_BRSVA	285-301	482-511				
PVGLF_BRSVC	484-513					
PVGLF_BRSVR	484-513					
PVGLF_CDVO	562-598					
PVGLF_HRSV1	484-513					
PVGLF_HRSVA	484-513					
PVGLF_HRSVL	484-513					
PVGLF_HRSVR	484-513					
PVGLF_MEASE	224-258	451-484				
PVGLF_MEASI	227-258	454-487				
PVGLF_MEASY	224-258	451-484				
PVGLF_MUMPM	448-474					
PVGLF_MUMPR	448-474					
PVGLF_MUMPS	5-38	448-474				
PVGLF_NDVI	132-185					
PVGLF_PHODV	531-565					
PVGLF_PI1HC	460-484					
PVGLF_PI3B	463-481					
PVGLF_PI3H4	453-481					
PVGLF_RINDK	220-262	447-480				
PVGLF_RINDL	220-262	447-480				
PVGLF_SEND5	460-488					
PVGLF_SENDF	460-488					
PVGLF_SENDH	460-488					
PVGLF_SENDJ	460-488					
PVGLF_SENDZ	460-488					
PVGLF_SV5	448-474					
PVGLF_TRTV	462-481					
PVGLG_H3VEB	327-364					
PVGLG_SYNV	524-553					
PVGLG_V3VIG	460-488					
PVGLG_V6VJO	457-492					
PVGLG_V6VO	450-488					
PVGLG_V6V6J	450-488					
PVGLH_HCMVA	691-719					
PVGLH_HCMVT	690-718					
PVGLH_H6V6G	640-677					
PVGLH_H6VE4	814-860					
PVGLH_H3VEB	807-843					
PVGLI_HCMVA	158-194					
PVGLM_BUNGE	197-227	438-468	982-1020	1048-1084		
PVGLM_BUNL7	180-220					
PVGLM_BUN3H	180-220	344-381				
PVGLM_BUNYW	183-228	434-472	823-864			
PVGLM_DUGBV	244-273	637-672	886-915	935-965	1403-1441	
PVGLM_HANTB	610-641	1081-1119				
PVGLM_HANTH	188-222	612-643	1082-1120			

PVGLM_HANTL	188-222	612-643	1083-1121		
PVGLM_HANTV	188-222	612-643	1083-1121		
PVGLM_PHV	616-649	1088-1121			
PVGLM_PTPV	848-882	1275-1309			
PVGLM_PUUMH	820-853	1092-1125			
PVGLM_PUUMS	820-853	1092-1125			
PVGLM_RVFV	820-853	830-863			
PVGLM_RVFVZ	820-853	830-863	1168-1185		
PVGLM_SEOUR	806-841	1082-1120			
PVGLM_SEOUS	810-841	1081-1119			
PVGLM_UUK	431-488	986-995			
PVGLP_BEV	1491-1528				
PVGLY_JUNIN	12-45				
PVGLY_LASSG	237-286				
PVGLY_LASSJ	238-288				
PVGLY_PIARV	12-50				
PVGLY_TACV	12-50				
PVGLY_TACV6	12-50	89-124			
PVGLY_TACV7	12-50	89-124			
PVGLY_TACVT	12-50	89-124			
PVGNB_CPMV	1627-1665				
PVGNM_BPMV	137-187	280-327	837-888		
PVGNM_CPMV	209-242	741-771			
PVGNM_CPSMV	50-88	478-515			
PVGNM_RCMV	788-789				
PVGP2_EBV	78-111				
PVGP3_EBV	78-111				
PVM1_REOVD	280-318	324-361			
PVM1_REOVL	280-318				
PVM21_REOVD	188-199				
PVM22_REOVD	188-199				
PVM2_REOVJ	188-199				
PVM2_REOVL	188-199				
PVM3_REOVD	333-384				
PVMAT_9V6	308-342				
PVMAT_TRTV	122-150				
PVME1_CVBM	84-102				
PVME1_CVHOC	84-102				
PVME1_CVMA5	85-103				
PVME1_CVMJH	85-103				
PVME1_CVTKE	84-102				
PVMEM_EBV	178-213				
PVMP_CERV	83-128				
PVMP_SOCMV	88-88	273-303			
PVMSA_HPBDB	201-238	288-302			
PVMSA_HPBDC	194-227	288-301			
PVMSA_HPBDU	167-190	231-284			

PVM3A_HPBDW	184-227	269-302			
PVM3A_HPBG6	208-243	271-307			
PVM3A_HPBHE	168-196	238-268			
PVM6A_HPBVO	70-98				
PVM3A_HPBV2	244-272				
PVM3A_HPBV4	244-272				
PVM3A_HPBV9	244-272				
PVM6A_HPBVA	233-261				
PVM6A_HPBVD	70-98				
PVM6A_HPBVI	233-261				
PVM3A_HPBVJ	233-261				
PVM6A_HPBVL	233-261				
PVM3A_HPBVN	70-98				
PVM6A_HPBVO	233-261				
PVM6A_HPBVP	244-272				
PVM6A_HPBVR	244-272				
PVM3A_HPBV3	70-98				
PVM3A_HPBVW	233-261				
PVM6A_HPBVY	233-261				
PVM6A_HPBVZ	233-261				
PVM3A_WHV1	207-241	269-305			
PVM6A_WHV59	212-246	274-310			
PVM3A_WHV7	212-246	274-310			
PVM6A_WHV8	212-246	274-310			
PVM3A_WHV8I	212-246	274-310			
PVM3A_WHVW8	125-161				
PVMT2_IAZ11	10-44				
PVMT8_MYXVL	6-34	141-170			
PVMT9_MYXVL	246-282				

5.3. SYNTHESIS OF PEPTIDES

The peptides of the invention may be synthesized or prepared by techniques well known in the art. See, for example, Creighton, 1983, Proteins: Structures and Molecular Principles, W.H. Freeman and Co., NY, which is incorporated herein by reference in its entirety. Short peptides, for example, can be synthesized on a solid support or in solution. Longer peptides amy be made using recombinant DNA techniques. Here, the nucleotide sequences encoding the peptides of the invention may be synthesized, and/or cloned, and expressed according to techniques well known to those of ordinary skill in the art. See, for example, Sambrook, et al., 1989, Molecular Cloning, A Laboratory Manual, Vols. 1-3, Cold Spring Harbor Press, NY.

The peptides of the invention may alternatively be synthesized such that one or more of the bonds which link the amino acid residues of the peptides are non-peptide bonds. These alternative non-peptide bonds may be formed by utilizing reactions well known to those in the art, and may include, but are not limited to imino, ester, hydrazide, semicarbazide, and azo bonds, to name but a few. In yet another embodiment of the invention, peptides comprising the sequences described above may be synthesized with additional chemical groups present at their amino and/or carboxy termini, such that, for example, the stability, bioavailability, and/or inhibitory activity of the peptides is enhanced. For example, hydrophobic groups such as carbobenzoxyl, dansyl, or t-butyloxycarbonyl groups, may be added to the peptides' amino termini. Likewise, an acetyl group or a 9-fluorenylmethoxy-carbonyl group may be placed at the peptides' amino termini. (See "X" in Tables I to IV, above.) Additionally, the hydrophobic group, t-

butyloxycarbonyl, or an amido group may be added to the peptides' carboxy termini. (See "Z" in Tables I to IV, above.) Further, the peptides of the invention may be synthesized such that their steric configuration is altered. For example, the D-isomer of one or more of the amino acid residues of the peptide may be used, rather than the usual L-isomer. Still further, at least one of the amino acid residues of the peptides of the invention may be substituted by one of the well known non-naturally occurring amino acid residues. Alterations such as these may serve to increase the stability, bioavailability and/or inhibitory action of the peptides of the invention.

Any of the peptides described above may, additionally, have a non-peptide macromolecular carrier group covalently attached to their amino and/or carboxy termini. Such macromolecular carrier groups may include, for example, lipid-fatty acid conjugates, polyethylene glycol, or carbohydrates. "X", in Tables I to IV, above, may therefore additionally represent any of the above macromolecular carrier groups covalently attached to the amino terminus of a peptide. Likewise, "Z", in Tables I to IV, may additionally represent any of the macromolecular carrier groups described above.

5.4. ASSAYS FOR ANTIVIRAL ACTIVITY

The antiviral activity exhibited by the peptides of the invention may be measured, for example, by easily performed in vitro assays, such as those described below, which can test the peptides' ability to inhibit syncytia formation, or their ability to inhibit infection by cell-free virus. Using these assays, such parameters as the relative antiviral activity of the peptides, exhibit against a given strain of virus and/or the strain specific inhibitory

activity of the peptide can be determined. A cell fusion assay may be utilized to test the peptides' ability to inhibit HIV-induced syncytia formation in vitro. Such an assay may comprise culturing uninfected CD-4$^+$ cells (such as Molt or CEM cells, for example) in the presence of chronically HIV-infected cells and a peptide to be assayed. For each peptide, a range of peptide concentrations may be tested. This range should include a control culture wherein no peptide has been added. Standard conditions for culturing, well known to those of ordinary skill in the art, are used. After incubation for an appropriate period (24 hours at 37°C, for example) the culture is examined microscopically for the presence of multinucleated giant cells, which are indicative of cell fusion and syncytia formation.

A reverse transcriptase (RT) assay may be utilized to test the peptides' ability to inhibit infection of CD-4$^+$ cells by cell-free HIV. Such an assay may comprise culturing an appropriate concentration (i.e., $TCID_{50}$) of virus and CD-4$^+$ cells in the presence of the peptide to be tested. Culture conditions well known to those in the art are used. As above, a range of peptide concentrations may be used, in addition to a control culture wherein no peptide has been added. After incubation for an appropriate period (e.g., 7 days) of culturing, a cell-free supernatant is prepared, using standard procedures, and tested for the present of RT activity as a measure of successful infection. The RT activity may be tested using standard techniques such as those described by, for example, Goff et al. (Goff, S. et al., 1981, J. Virol. 38:239-248) and/or Willey et al. (Willey, R. et al., 1988, J. Virol. 62:139-147). These references are incorporated herein by reference in their entirety.

Standard methods which are well-known to those of skill in the art may be utilized for assaying non-retroviral activity. See, for example, Pringle et al. (Pringle, C.R. et al., 1985, J. Medical Virology 17:377-386) for a discussion of respiratory syncytial virus and parainfluenza virus activity assay techniques. Further, see, for example, "Zinsser Microbiology", 1988, Joklik, W.K. et al., eds., Appleton & Lange, Norwalk, CT, 19th ed., for a general review of such techniques. These references are incorporated by reference herein in its entirety.

5.5. USES OF THE PEPTIDES OF THE INVENTION

The DP-178 (SEQ ID:1) peptides of the invention, and DP-178 fragments, analogs, and homologs, exhibit potent antiviral activity. The DP-107-like and DP-178-like peptides of the invention preferably exhibit antiviral activity. As such, the peptides may be used as inhibitors of human and non-human viral and retroviral, especially HIV, transmission to uninfected cells.

The human retroviruses whose transmission may be inhibited by the peptides of the invention include, but are not limited to all strains of HIV-1 and HIV-2 and the human T-lymphocyte viruses (HTLV-I and II). The non-human retroviruses whose transmission may be inhibited by the peptides of the invention include, but are not limited to bovine leukosis virus, feline sarcoma and leukemia viruses, simian immunodeficiency, sarcoma and leukemia viruses, and sheep progress pneumonia viruses.

Non retroviral viruses whose transmission may be inhibited by the peptides of the invention include, but are not limited to human respiratory syncytial virus, canine distemper virus, newcastle disease virus, human parainfluenza virus, and influenza

viruses. Further, any virus or retrovirus containing peptides listed in Tables V through X above, may be inhibited by the peptides of the invention.

As discussed more fully, below, in Section 5.5.1 and in the Example presented, below, in Section 8, DP-107 and DP-178, and DP-107-like and DP-178-like peptides form non-covalent protein-protein interactions which are required for normal activity of the virus. Thus, the peptides of the invention may also be utilized as components in assays for the identification of compounds that interfere with such protein-protein interactions and may, therefore, act as antiviral agents. These assays are discussed, below, in Section 5.5.1.

5.5.1. ANTIVIRAL COMPOUND SCREENING SCREENING ASSAYS FOR COMPOUNDS THAT INTERACT WITH THE PKD1 GENE PRODUCT

As demonstrated in the Example presented in Section 8, below, DP-107 and DP-178 portions of the TM protein gp41 form non-covalent protein-protein intereactions. As also demonstrated, the maintenance of such interactions is necessary for normal viral infectivity. Thus, compounds which bind DP-107, bind DP-178, and/or act to disrupt normal DP-107/DP-178 protein-protein interactions may act as patent antiviral agents. Described below are assays for the identification of such compounds. Note that, while, for case and clarity of discussion, DP-107 and DP-178 peptides will be used as components of the assays described, but it is to be understood that any of the DP-107-like or DP-178-like peptides described, above, in Sections 5.1 and 5.2 may also be utilized as part of these screens for antiviral compounds.

Compounds which may be tested for an ability to bind DP-107, DP-178, and/or disrupt DP-107/DP-178 interactions, and which therefore, potentially

represent antiviral compounds, include, but are not limited to, peptides made of D- and/or L-configuration amino acids (in, for example, the form of random peptide libraries; see Lam, K.S. et al., 1991, Nature 354:82-84), phosphopeptides (in, for example, the form of random or partially degenerate, directed phosphopeptide libraries; see, for example, Songyang, Z. et al., 1993, Cell 72:767-778), antibodies, and small organic or inorganic molecules. Synthetic compounds, natural products, and other sources of potentially effective materials may be screened in a variety of ways, as described in this Section. The compounds, antibodies, or other molecules identified may be tested for an ability to inhibit viral activity, utilizing, for example, viral assays such as those described, above, in Section 5.4.

Among the peptides which may be tested are soluble peptides comprising DP-107 and/or DP-178 domains, and peptides comprising DP-107 and/or DP-178 domains having one or more mutations within one or both of the domains, such as the M41-P peptide described, below, in the Example presented in Section 8, which contains a isoleucine to proline mutation within the DP-178 sequence.

In one embodiment of such screening methods is a method for identifying a compound to be tested for antiviral ability comprising:

(a) exposing at least one compound to a peptide comprising a DP-107 peptide for a time sufficient to allow binding of the compound to the DP-107 peptide;

(b) removing non-bound compounds; and

(c) determining the presence of the compound bound to the DP-107 peptide,

thereby identifying an agent to be tested for antiviral ability.

In a second embodiment of such screening methods is a method for identifying a compound to be tested for antiviral ability comprising:

(a) exposing at least one compound to a peptide comprising a DP-178 peptide for a time sufficient to allow binding of the compound to the DP-178 peptide;

(b) removing non-bound compounds; and

(c) determining the presence of the compound bound to the DP-178 peptide,

thereby identifying an agent to be tested for antiviral ability.

One method utilizing these types of approaches that may be pursued in the isolation of such DP-107-binding or DP-178-binding compounds is an assay which would include the attachment of either the DP-107 or the DP-178 peptide to a solid matrix, such as, for example, agarose or plastic beads, microtiter plate wells, petri dishes, or membranes composed of, for example, nylon or nitrocellulose. In such an assay system, either the DP-107 or DP-178 protein may be anchored onto a solid surface, and the compound, or test substance, which is not anchored, is labeled, either directly or indirectly. In practice, microtiter plates are conveniently utilized. The anchored component may be immobilized by non-covalent or covalent attachments. Non-covalent attachment may be accomplished simply by coating the solid surface with a solution of the protein and drying. Alternatively, an immobilized antibody, preferably a monoclonal antibody, specific for the protein may be used to anchor the protein to the solid surface. The surfaces may be prepared in advance and stored.

In order to conduct the assay, the labeled compound is added to the coated surface containing the anchored DP-107 or DP-178 peptide. After the reaction

is complete, unreacted components are removed (e.g., by washing) under conditions such that any complexes formed will remain immobilized on the solid surface. The detection of complexes anchored on the solid surface can be accomplished in a number of ways. Where the compound is pre-labeled, the detection of label immobilized on the surface indicates that complexes were formed. Where the labeled component is not pre-labeled, an indirect label can be used to detect complexes anchored on the surface; e.g., using a labeled antibody specific for the compound (the antibody, in turn, may be directly labeled or indirectly labeled with a labeled anti-Ig antibody).

Alternatively, such an assay can be conducted in a liquid phase, the reaction products separated from unreacted components, and complexes detected; e.g., using an immobilized antibody specific for DP-107 or DP-178, whichever is appropriate for the given assay, or ab antibody specific for the compound, i.e., the test substance, in order to anchor any complexes formed in solution, and a labeled antibody specific for the other member of the complex to detect anchored complexes.

By utilizing procedures such as this, large numbers of types of molecules may be simultaneously screened for DP-107 or DP-178-binding capability, and thus potential antiviral activity.

Further, compounds may be screened for an ability to inhibit the formation of or, alternatively, disrupt DP-107/DP-178 complexes. Such compounds may then be tested for antiviral capability. For ease of description, DP-107 and DP-178 will be referred to as "binding partners." Compounds that disrupt such interactions may exhibit antiviral activity. Such compounds may include, but are not limited to

molecules such as antibodies, peptides, and the like described above.

The basic principle of the assay systems used to identify compounds that interfere with the interaction between the DP-107 and DP-178 peptides involves preparing a reaction mixture containing peptides under conditions and for a time sufficient to allow the two peptides to interact and bind, thus forming a complex. In order to test a compound for disruptive activity, the reaction is conducted in the presence and absence of the test compound, i.e., the test compound may be initially included in the reaction mixture, or added at a time subsequent to the addition of one of the binding partners; controls are incubated without the test compound or with a placebo. The formation of any complexes between the binding partners is then detected. The formation of a complex in the control reaction, but not in the reaction mixture containing the test compound indicates that the compound interferes with the interaction of the DP-107 and DP-178 peptides.

The assay for compounds that interfere with the interaction of the binding partners can be conducted in a heterogeneous or homogeneous format. Heterogeneous assays involve anchoring one of the binding partners onto a solid phase and detecting complexes anchored on the solid phase at the end of the reaction. In homogeneous assays, the entire reaction is carried out in a liquid phase. In either approach, the order of addition of reactants can be varied to obtain different information about the compounds being tested. For example, test compounds that interfere with the interaction between the binding partners, e.g., by competition, can be identified by conducting the reaction in the presence of the test substance; i.e., by adding the test

substance to the reaction mixture prior to or simultaneously with the binding partners. On the other hand, test compounds that disrupt preformed complexes, e.g. compounds with higher binding constants that displace one of the binding partners from the complex, can be tested by adding the test compound to the reaction mixture after complexes have been formed. The various formats are described briefly below.

In a heterogeneous assay system, one binding partner, e.g., either the DP-107 or DP-178 peptide, is anchored onto a solid surface, and its binding partner, which is not anchored, is labeled, either directly or indirectly. In practice, microtiter plates are conveniently utilized. The anchored species may be immobilized by non-covalent or covalent attachments. Non-covalent attachment may be accomplished simply by coating the solid surface with a solution of the protein and drying. Alternatively, an immobilized antibody specific for the protein may be used to anchor the protein to the solid surface. The surfaces may be prepared in advance and stored.

In order to conduct the assay, the binding partner of the immobilized species is added to the coated surface with or without the test compound. After the reaction is complete, unreacted components are removed (e.g., by washing) and any complexes formed will remain immobilized on the solid surface. The detection of complexes anchored on the solid surface can be accomplished in a number of ways. Where the binding partner was pre-labeled, the detection of label immobilized on the surface indicates that complexes were formed. Where the binding partner is not pre-labeled, an indirect label can be used to detect complexes anchored on the surface; e.g., using a labeled antibody specific for

the binding partner (the antibody, in turn, may be directly labeled or indirectly labeled with a labeled anti-Ig antibody). Depending upon the order of addition of reaction components, test compounds which inhibit complex formation or which disrupt preformed complexes can be detected.

Alternatively, the reaction can be conducted in a liquid phase in the presence or absence of the test compound, the reaction products separated from unreacted components, and complexes detected; e.g., using an immobilized antibody specific for one binding partner to anchor any complexes formed in solution, and a labeled antibody specific for the other binding partner to detect anchored complexes. Again, depending upon the order of addition of reactants to the liquid phase, test compounds which inhibit complex or which disrupt preformed complexes can be identified.

In an alternate embodiment of the invention, a homogeneous assay can be used. In this approach, a preformed complex of the DP-107 and DP-178 peptides is prepared in which one of the binding partners is labeled, but the signal generated by the label is quenched due to complex formation (see, e.g., U.S. Patent No. 4,109,496 by Rubenstein which utilizes this approach for immunoassays). The addition of a test substance that competes with and displaces one of the binding partners from the preformed complex will result in the generation of a signal above background. In this way, test substances which disrupt DP-107/ DP-178 protein-protein interaction can be identified.

5.5 PHARMACEUTICAL FORMULATIONS, DOSAGES AND MODES OF ADMINISTRATION

With respect to HIV, the peptides of the invention may be used as a therapeutic in the

treatment of AIDS. The peptides of the invention may be administered using techniques well known to those in the art. Preferably, agents are formulated and administered systemically. Techniques for formulation and administration may be found in "Remington's Pharmaceutical Sciences", 18th ed., 1990, Mack Publishing Co., Easton, PA. Suitable routes may include oral, rectal, transmucosal, or intestinal administration; parenteral delivery, including intramuscular, subcutaneous, intramedullary injections, as well as intrathecal, direct intraventricular, intravenous, intraperitoneal, intranasal, or intraocular injections, just to name a few. Most preferably, administration is intravenous. For injection, the agents of the invention may be formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hanks' solution, Ringer's solution, or physiological saline buffer. For such transmucosal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art.

In addition, the peptides may be used as a prophylactic measure in previously uninfected individuals after acute exposure to an HIV virus. Examples of such prophylactic use of the peptides may include, but are not limited to, prevention of virus transmission from mother to infant and other settings where the likelihood of HIV transmission exists, such as, for example, accidents in health care settings wherein workers are exposed to HIV-containing blood products. The peptides of the invention in such cases may serve the role of a prophylactic vaccine, wherein the host raises antibodies against the peptides of the invention, which then serve to neutralize HIV viruses by, for example, inhibiting further HIV infection.

Administration of the peptides of the invention as a prophylactic vaccine, therefore, would comprise administering to a host a concentration of peptides effective in raising an immune response which is sufficient to neutralize HIV, by, for example, inhibiting HIV ability to infect cells. The exact concentration will depend upon the specific peptide to be administered, but may be determined by using standard techniques for assaying the development of an immune response which are well known to those of ordinary skill in the art. The peptides to be used as vaccines are usually administered intramuscularly.

The peptides may be formulated with a suitable adjuvant in order to enhance the immunological response. Such adjuvants may include, but are not limited to mineral gels such as aluminum hydroxide; surface active substances such as lysolecithin, pluronic polyols, polyanions; other peptides; oil emulsions; and potentially useful human adjuvants such as BCG and Corynebacterium parvum. Many methods may be used to introduce the vaccine formulations described here. These methods include but are not limited to oral, intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, and intranasal routes.

Alternatively, an effective concentration of polyclonal or monoclonal antibodies raised against the peptides of the invention may be administered to a host so that no uninfected cells become infected by HIV. The exact concentration of such antibodies will vary according to each specific antibody preparation, but may be determined using standard techniques well known to those of ordinary skill in the art. Administration of the antibodies may be accomplished using a variety of techniques, including, but not limited to those described in this section.

Effective dosages of the peptides of the invention to be administered may be determined through procedures well known to those in the art which address such parameters as biological half-life, bioavailability, and toxicity. Given the data presented below in Section 6, DP-178, for example, may prove efficacious in vivo at doses required achieve circulating levels of 10ng per ml of peptide.

A therapeutically effective dose refers to that amount of the compound sufficient to result in amelioration of symptoms or a prolongation of survival in a patient. Toxicity and therapeutic efficacy of such compounds can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, e.g., for determining the LD50 (the dose lethal to 50% of the population) and the ED50 (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio LD50/ED50. Compounds which exhibit large therapeutic indices are preferred. The data obtained from these cell culture assays and animal studies can be used in formulating a range of dosage for use in humans. The dosage of such compounds lies preferably within a range of circulating concentrations that include the ED50 with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized. For any compound used in the method of the invention, the therapeutically effective dose can be estimated initially from cell culture assays. A dose may be formulated in animal models to achieve a circulating plasma concentration range that includes the IC50 (i.e., the concentration of the test compound which achieves a half-maximal disruption of the PTK/adaptor

protein complex, or a half-maximal inhibition of the cellular level and/or activity of a complex component) as determined in cell culture. Such information can be used to more accurately determine useful doses in humans. Levels in plasma may be measured, for example, by high performance liquid chromatography (HPLC).

The exact formulation, route of administration and dosage can be chosen by the individual physician in view of the patient's condition. (See e.g. Fingl et al., 1975, in "The Pharmacological Basis of Therapeutics", Ch. 1 p1).

It should be noted that the attending physician would know how to and when to terminate, interrupt, or adjust administration due to toxicity, or to organ dysfunctions. Conversely, the attending physician would also know to adjust treatment to higher levels if the clinical response were not adequate (precluding toxicity). The magnitude of an administrated dose in the management of the oncogenic disorder of interest will vary with the severity of the condition to be treated and to the route of administration. The dose and perhaps dose frequency, will also vary according to the age, body weight, and response of the individual patient. A program comparable to that discussed above may be used in veterinary medicine.

As demonstrated in the Example presented below in Section 6, the antiviral activity of the peptides of the invention may show a pronounced type and subtype specificity, i.e., specific peptides may be effective in inhibiting the activity of only specific viruses. This feature of the invention presents many advantages. One such advantage, for example, lies in the field of diagnostics, wherein one can use the antiviral specificity of the peptide of the invention to ascertain the identity of a viral isolate. With

respect to HIV, one may easily determine whether a viral isolate consists of an HIV-1 or HIV-2 strain. For example, uninfected CD-4$^+$ cells may be co-infected with an isolate which has been identified as containing HIV the DP-178 (SEQ ID:1) peptide, after which the retroviral activity of cell supernatents may be assayed, using, for example, the techniques described above in Section 5.2. Those isolates whose retroviral activity is completely or nearly completely inhibited contain HIV-1. Those isolates whose viral activity is unchanged or only reduced by a small amount, may be considered to not contain HIV-1. Such an isolate may then be treated with one or more of the other DP-178 peptides of the invention, and subsequently be tested for its viral activity in order to determine the identify of the viral isolate.

Use of pharmaceutically acceptable carriers to formulate the compounds herein disclosed for the practice of the invention into dosages suitable for systemic administration is within the scope of the invention. With proper choice of carrier and suitable manufacturing practice, the compositions of the present invention, in particular, those formulated as solutions, may be administered parenterally, such as by intravenous injection. The compounds can be formulated readily using pharmaceutically acceptable carriers well known in the art into dosages suitable for oral administration. Such carriers enable the compounds of the invention to be formulated as tablets, pills, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a patient to be treated.

Pharmaceutical compositions suitable for use in the present invention include compositions wherein the active ingredients are contained in an effective amount to achieve its intended purpose. Determination

of the effective amounts is well within the capability of those skilled in the art, especially in light of the detailed disclosure provided herein.

In addition to the active ingredients, these pharmaceutical compositions may contain suitable pharmaceutically acceptable carriers comprising excipients and auxiliaries which facilitate processing of the active compounds into preparations which can be used pharmaceutically. The preparations formulated for oral administration may be in the form of tablets, dragees, capsules, or solutions.

The pharmaceutical compositions of the present invention may be manufactured in a manner that is itself known, e.g., by means of conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping or lyophilizing processes.

Pharmaceutical formulations for parenteral administration include aqueous solutions of the active compounds in water-soluble form. Additionally, suspensions of the active compounds may be prepared as appropriate oily injection suspensions. Suitable lipophilic solvents or vehicles include fatty oils such as sesame oil, or synthetic fatty acid esters, such as ethyl oleate or triglycerides, or liposomes. Aqueous injection suspensions may contain substances which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Optionally, the suspension may also contain suitable stabilizers or agents which increase the solubility of the compounds to allow for the preparation of highly concentrated solutions.

Pharmaceutical preparations for oral use can be obtained by combining the active compounds with solid excipient, optionally grinding a resulting mixture, and processing the mixture of granules, after adding

suitable auxiliaries, if desired, to obtain tablets or dragee cores. Suitable excipients are, in particular, fillers such as sugars, including lactose, sucrose, mannitol, or sorbitol; cellulose preparations such as, for example, maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, and/or polyvinylpyrrolidone (PVP). If desired, disintegrating agents may be added, such as the cross-linked polyvinyl pyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate.

Dragee cores are provided with suitable coatings. For this purpose, concentrated sugar solutions may be used, which may optionally contain gum arabic, talc, polyvinyl pyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments may be added to the tablets or dragee coatings for identification or to characterize different combinations of active compound doses.

Pharmaceutical preparations which can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The push-fit capsules can contain the active ingredients in admixture with filler such as lactose, binders such as starches, and/or lubricants such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active compounds may be dissolved or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols. In addition, stabilizers may be added.

6. EXAMPLE: DP-178 (SEQ ID:1) IS A POTENT INHIBITOR OF HIV-1 INFECTION

In this example, DP-178 (SEQ ID:1) is shown to be a potent inhibitor of HIV-1 mediated CD-4$^+$ cell-cell fusion and infection by cell free virus. In the fusion assay, this peptide completely blocks virus induced syncytia formation at concentrations of from 1-10 ng/ml. In the infectivity assay the inhibitory concentration is somewhat higher, blocking infection at 90ng/ml. It is further shown that DP-178 (SEQ ID:1) shows that the antiviral activity of DP-178 (SEQ ID:1) is highly specific for HIV-1. Additionally, a synthetic peptide, DP-185 (SEQ ID:3), representing a HIV-1-derived DP-178 homolog is also found to block HIV-1-mediated syncytia formation.

6.1. MATERIALS AND METHODS

6.1.1. PEPTIDE SYNTHESIS

Peptides were synthesized using Fast Moc chemistry on an Applied Biosystems Model 431A peptide synthesizer. Amidated peptides were prepared using Rink resin (Advanced Chemtech) while peptides containing free carboxy termini were synthesized on Wang (p-alkoxy-benzyl-alcohol) resin (Bachem). First residues were double coupled to the appropriate resin and subsequent residues were single coupled. Each coupling step was followed by acetic anhydride capping. Peptides were cleaved from the resin by treatment with trifluoracetic acid (TFA) (10ml), H_2O (0.5ml), thioanisole (0.5ml), ethanedithiol (0.25ml), and crystalline phenol (0.75g). Purification was carried out by reverse phase HPLC. Approximately 50mg samples of crude peptide were chromatographed on a Waters Delta Pak C18 column (19mm x 30cm, 15μ spherical) with a linear gradient; H_2O/acetonitrile

0.1% TFA. Lyophilized peptides were stored desiccated and peptide solutions were made in water at about 1mg/ml. Electrospray mass spectrometry yielded the following results: DP-178 (SEQ ID:1):4491.87 (calculated 4491.94); DP-180 (SEQ ID:2):4491.45 (calculated 4491.94); DP-185 (SEQ ID:3):not done (calculated 4546.97).

6.1.2. VIRUS

The HIV-1_{LAI} virus was obtained from R. Gallo (Popovic, M. et al., 1984, Science 224:497-508) and propagated in CEM cells cultured in RPMI 1640 containing 10% fetal calf serum. Supernatant from the infected CEM cells was passed through a 0.2μm filter and the infectious titer estimated in a microinfectivity assay using the AA5 cell line to support virus replication. For this purpose, 25μl of serial diluted virus was added to 75μl AA5 cells at a concentration of 2 x 10^5/ml in a 96-well microtitre plate. Each virus dilution was tested in triplicate. Cells were cultured for eight days by addition of fresh medium every other day. On day 8 post infection, supernatant samples were tested for virus replication as evidenced by reverse transcriptase activity released to the supernatant. The $TCID_{50}$ was calculated according to the Reed and Muench formula (Reed, L.J. et al., 1938, Am. J. Hyg. 27:493-497). The titer of the HIV-1_{LAI} and HIV-1_{MN} stocks used for these studies, as measured on the AA5 cell line, was approximately 1.4 x 10^6 and 3.8 x 10^4 $TCID_{50}$/ml, respectively.

6.1.3. CELL FUSION ASSAY

Approximately 7 x 10^4 Molt cells were incubated with 1 x 10^4 CEM cells chronically infected with the HIV-1_{LAI} virus in 96-well plates (one-half area cluster plates; Costar, Cambridge, MA) in a final volume of

100μl culture medium as previously described (Matthews, T.J. et al., 1987, Proc. Natl. Acad. Sci. USA 84: 5424-5428). Peptide inhibitors were added in a volume of 10μl and the cell mixtures were incubated for 24 hr. at 37°C. At that time, multinucleated giant cells were estimated by microscopic examination at a 40x magnification which allowed visualization of the entire well in a single field.

6.1.4. CELL FREE VIRUS INFECTION ASSAY

Synthetic peptides were incubated at 37°C with either 247 $TCID_{50}$ (for experiment depicted in FIG. 2), or 62 $TCID_{50}$ (for experiment depicted in FIG.3) units of HIV-1_{LAI} virus or 25 $TCID_{50}$ units of HIV-2_{NIH2} and CEM $CD4^+$ cells at peptide concentrations of 0, 0.04, 0.4, 4.0, and 40μg/ml for 7 days. The resulting reverse transcriptase (RT) activity in counts per minute was determined using the assay described, below, in Section 6.1.5. See, Reed, L.J. et al., 1938, Am. J. Hyg. 27: 493-497 for an explanation of $TCID_{50}$ calculations.

6.1.5. REVERSE TRANSCRIPTASE ASSAY

The micro-reverse transcriptase (RT) assay was adapted from Goff et al. (Goff, S. et al., 1981, J. Virol. 38:239-248) and Willey et al. (Willey, R. et al., 1988, J. Virol. 62:139-147). Supertanants from virus/cell cultures are adjusted to 1% Triton-X100. A 10μl sample of supernatant was added to 50μl of RT cocktail in a 96-well U-bottom microtitre plate and the samples incubated at 37°C for 90 min. The RT cocktail contained 75mM KCl, 2mM dithiothreitol, 5mM $MgCl_2$, 5μg/ml poly A (Pharmacia, cat. No. 27-4110-01), 0.25 units/ml oligo dT (Pharmacia, cat. No. 27-7858-01), 0.05% NP40, 50mM Tris-HCl, pH 7.8, 0.5μM non-

radioactive dTTP, and 10μCi/ml ^{32}P-dTTP (Amersham, cat. No. PB.10167).

After the incubation period, 40μl of reaction mixture was applied to a Schleicher and Schuell (S+S) NA45 membrane (or DE81 paper) saturated in 2 x SSC buffer (0.3M NaCl and 0.003M sodium citrate) held in a S+S Minifold over one sheet of GB003 (S+S) filter paper, with partial vacuum applied. Each well of the minifold was washed four times with 200μl 2xSSC, under full vacuum. The membrane was removed from the minifold and washed 2 more times in a pyrex dish with an excess of 2xSSC. Finally, the membrane was drained on absorbent paper, placed on Whatman #3 paper, covered with Saran wrap, and exposed to film overnight at -70°C.

6.2. RESULTS

6.2.1. PEPTIDE INHIBITION OF INFECTED CELL-INDUCED SYNCYTIA FORMATION

The initial screen for antiviral activity assayed peptides' ability to block syncytium formation induced by overnight co-cultivation of uninfected Molt4 cells with chronically HIV-1 infected CEM cells. The results of several such experiments are presented herein. In the first of these experiments, serial DP-178 (SEQ ID:1) peptide concentrations between 10μg/ml and 12.5ng/ml were tested for blockade of the cell fusion process. For these experiments, CEM cells chronically infected with either HIV-1_{LAI}, HIV-1_{MN}, HIV-1_{RF}, or HIV-1_{SF2} virus were cocultivated overnight with uninfected Molt 4 cells. The results (FIG. 4) show that DP-178 (SEQ ID:1) afforded complete protection against each of the HIV-1 isolates down to the lowest concentration of DP-178 (SEQ ID:1) used. For HIV_{LAI} inhibition, the lowest concentration tested was

12.5ng/ml; for all other HIV-1 viruses, the lowest concentration of DP-178 (SEQ ID:1) used in this study was 100ng/ml. A second peptide, DP-180 (SEQ ID:2), containing the same amino acid residues as DP-178 (SEQ ID:1) but arranged in a random order exhibited no evidence of anti-fusogenic activity even at the high concentration of 40μg/ml (FIG. 4). These observations indicate that the inhibitory effect of DP-178 (SEQ ID:1) is primary sequence-specific and not related to non-specific peptide/protein interactions. The actual endpoint (i.e., the lowest effective inhibitory concentration) of DP-178 inhibitory action is within the range of 1-10 ng/ml.

The next series of experiments involved the preparation and testing of a DP-178 (SEQ ID:1) homolog for its ability to inhibit HIV-1-induced syncytia formation. As shown in FIG. 1, the sequence of DP-185 (SEQ ID:3) is slightly different from DP-178 (SEQ ID:1) in that its primary sequence is taken from the $HIV\text{-}1_{SF2}$ isolate and contains several amino acid differences relative to DP-178 (SEQ ID:1) near the N terminus. As shown in FIG. 4, DP-185 (SEQ ID:3), exhibits inhibitory activity even at 312.5ng/ml, the lowest concentration tested.

The next series of experiments involved a comparison of DP-178 (SEQ ID:1) HIV-1 and HIV-2 inhibitory activity. As shown in FIG. 5, DP-178 (SEQ ID:1) blocked HIV-1-mediated syncytia formation at peptide concentrations below 1ng/ml. DP-178 (SEQ ID:1) failed, however, to block HIV-2 mediated syncytia formation at concentrations as high as 10μg/ml. This striking 4 log selectivity of DP-178 (SEQ ID:1) as an inhibitor of HIV-1-mediated cell fusion demonstrates an unexpected HIV-1 specificity in the action of DP-178 (SEQ ID:1). DP-178 (SEQ ID:1) inhibition of HIV-1-mediated cell fusion, but the

peptide's inability to inhibit HIV-2 medicated cell fusion in the same cell type at the concentrations tested provides further evidence for the high degree of selectivity associated with the antiviral action of DP-178 (SEQ ID:1).

6.2.2. PEPTIDE INHIBITION OF INFECTION BY CELL-FREE VIRUS

DP-178 (SEQ ID:1) was next tested for its ability to block CD-4$^+$ CEM cell infection by cell free HIV-1 virus. The results, shown in FIG. 2, are from an experiment in which DP-178 (SEQ ID:1) was assayed for its ability to block infection of CEM cells by an HIV-1_{LAI} isolate. Included in the experiment were three control peptides, DP-116 (SEQ ID:9), DP-125 (SEQ ID:8), and DP-118 (SEQ ID:10). DP-116 (SEQ ID:9) represents a peptide previously shown to be inactive using this assay, and DP-125 (SEQ ID:8; Wild, C. et al., 1992, Proc. Natl. Acad, Sci. USA 89:10,537) and DP-118 (SEQ ID:10) are peptides which have previously been shown to be active in this assay. Each concentration (0, 0.04, 0.4, 4, and 40μg/ml) of peptide was incubated with 247 $TCID_{50}$ units of HIV-1_{LAI} virus and CEM cells. After 7 days of culture, cell-free supernatant was tested for the presence of RT activity as a measure of successful infection. The results, shown in FIG. 2, demonstrate that DP-178 (SEQ ID:1) inhibited the de novo infection process mediated by the HIV-1 viral isolate at concentrations as low as 90ng/ml (IC50=90ng/ml). In contrast, the two positive control peptides, DP-125 (SEQ: ID:8) and DP-118 (SEQ ID:10), had over 60-fold higher IC50 concentrations of approximately 5μg/ml.

In a separate experiment, the HIV-1 and HIV-2 inhibitory action of DP-178 (SEQ ID:1) was tested with CEM cells and either HIV-1_{LAI} or HIV-2_{NIHZ}. 62 $TCID_{50}$

HIV-1_{LAI} or 25 $GCID_{50}$ HIV-2_{NIHZ} were used in these experiments, and were incubated for 7 days. As may be seen in FIG. 3, DP-178 (SEQ ID:1) inhibited HIV-1 infection with an IC50 of about 31ng/ml. In contrast, DP-178 (SEQ ID:1) exhibited a much higher IC50 for HIV-2_{NIHZ}, thus making DP-178 (SEQ ID:1) two logs more potent as a HIV-1 inhibitor than a HIV-2 inhibitor. This finding is consistent with the results of the fusion inhibition assays described, above, in Section 6.2.1, and further supports a significant level of selectivity (i.e., for HIV-1 over HIV-2).

7. EXAMPLE: THE HIV-1 INHIBITOR, DP-178 (SEQ ID:1) IS NON-CYTOXIC

In this Example, the 36 amino acid synthetic peptide inhibitor DP-178 (SEQ ID:1) is shown to be non-cytotoxic to cells in culture, even at the highest peptide concentrations (40μg/ml) tested.

7.1. MATERIALS AND METHODS

Cell proliferation and toxicity assay: Approximately $3.8x10^5$ CEM cells for each peptide concentration were incubated for 3 days at 37°C in T25 flasks. Peptides tested were DP-178 (SEQ ID:1) and DP-116 (SEQ ID:9), as described in FIG. 1. The concentrations of each peptide used were 0, 2.5, 10, and 40μg/ml. Cell counts were taken at incubation times of 0, 24, 48, and 72 hours.

7.2. RESULTS

Whether the potent HIV-1 inhibitor DP-178 (SEQ ID:1) exhibited any cytotoxic effects was assessed by assaying the peptide's effects on the proliferation and viability of cells in culture. CEM cells were incubated in the presence of varying concentrations of DP-178 (SEQ ID:1), and DP-116 (SEQ ID:9), a peptide

previously shown to be ineffective as a HIV inhibitor (Wild, C. et al., 1992, Proc. Natl. Acad. Sci. USA 89:10,537-10,541). Additionally, cells were incubated in the absence of either peptide.

The results of the cytoxicity study demonstrate that DP-178 (SEQ ID:1) exhibits no cytotoxic effects on cells in culture. As can be seen, below, in Table XI, even the proliferation and viability characteristics of cells cultured for 3 days in the presence of the highest concentration of DP-178 (SEQ ID:1) tested (40μg/ml) do not significantly differ from the DP-116 (SEQ ID:9) or the no-peptide controls. The cell proliferation data is also represented in graphic form in FIG. 6. As was demonstrated in the Working Example presented above in Section 6, DP-178 (SEQ ID:1) completely inhibits HIV-1 mediated syncytia formation at peptide concentrations between 1 and 10ng/ml, and completely inhibits cell-free viral infection at concentrations of at least 90ng/ml. Thus, this study demonstrates that even at peptide concentrations greater than 3 log higher than the HIV inhibitory dose, DP-178 (SEQ ID:1) exhibits no cytoxic effects.

TABLE XI

Peptide	Peptide Concentration μg/ml	% Viability at time (hours) 0	24	48	72
DP178 (SEQ ID:1)	40	98	97	95	97
	10	98	97	98	98
	2.5	98	93	96	96

DP116 (SEQ ID:9)	40	98	95	98	97
	10	98	95	93	98
	2.5	98	96	98	99
No Peptide	0	98	97	99	98

8. EXAMPLE: THE INTERACTION OF DP178 AND DP107

Soluble recombinant forms of gp41 used in the example described below provide evidence that the DP178 peptide associates with a distal site on gp41 whose interactive structure is influenced by the DP107 leucine zipper motif. A single mutation disrupting the coiled-coil structure of the leucine zipper domain transformed the soluble recombinant gp41 protein from an inactive to an active inhibitor of HIV-1 fusion. This transformation may result from liberation of the potent DP178 domain from a molecular clasp with the leucine zipper, DP107, determinant. The results also indicate that the anti-HIV activity of various gp41 derivatives (peptides and recombinant proteins) may be due to their ability to form complexes with viral gp41 and interfere with its fusogenic process.

8.1. MATERIALS AND METHODS

8.1.1. CONSTRUCTION OF FUSION PROTEINS AND GP41 MUTANTS

Construction of fusion proteins and mutants shown in FIG. 7 was accomplished as follows: the DNA sequence corresponding to the extracellular domain of gp41 (540-686) was cloned into the Xmn I site of the expression vector pMal-p2 (New England Biolab) to give M41. The gp41 sequence was amplified from pgtat

(Malim et al., 1988, Nature 355: 181-183) by using polymerase chain reaction (PCR) with upstream primer 5'-ATGACGCTGACGGTACAGGCC-3' (primer A) and downstream primer 5'-TGACTAAGCTTAATACCACAGCCAATTTGTTAT-3' (primer B). M41-P was constructed by using the T7-Gen in vitro mutagenesis kit from United States Biochemicals (USB) following the supplier's instructions. The mutagenic primer (5'-GGAGCTGCTTGGGGCCCCAGAC-3') introduces an Ile to Pro mutation in M41 at position 578. M41Δ107 was made using a deletion mutagenic primer 5'-CCAAATCCCCAGGAGCTGCTCGAGCTGCACTATACCAGAC-3' (primer C) following the USB T7-Gen mutagenesis protocol. M41Δ178 was made by cloning the DNA fragment corresponding to gp41 amino acids 540-642 into the Xmn I site of pMal-p2. Primer A and 5'-ATAGCTTCTAGATTAATTGTTAATTTCTCTGTCCC-3' (primer D) were used in the PCR with the template pgtat to generate the inserted DNA fragments. M41-P was used as the template with primer A and D in PCR to generate M41-PΔ178. All inserted sequences and mutated residues were checked by restriction enzyme analysis and confirmed by DNA sequencing.

8.1.2. PURIFICATION AND CHARACTERIZATION OF FUSION PROTEINS

The fusion proteins were purified according to the protocol described in the manufacturer's brochure of protein fusion and purification systems from New England Biolabs (NEB). Fusion proteins (10 ng) were analyzed by electrophoresis on 8% SDS polyacrylamide gels. Western blotting analysis was performed as described by Sambrook et al, 1989, Molecular Cloning: A Laboratory Manual, 2d Ed, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, Ch. 18, pp. 64-75. An HIV-1 positive serum diluted 1000-fold,

or a human Fab derived from repertoire cloning was used to react with the fusion proteins. The second antibody was HRP-conjugated goat antihuman Fab. An ECL Western blotting detection system (Amersham) was used to detect the bound antibody. A detailed protocol for this detection system was provided by the manufacturer. Rainbow molecular weight marker (Amersham) were used to estimate the size of fusion proteins.

8.1.3. CELL FUSION ASSAYS FOR ANTI-HIV ACTIVITY

Cell fusion assays were performed as previously described (Matthews et al., 1987, Proc. Natl. Acad. Sci. USA 84: 5424-5481). CEM cells (7 X 10^4) were incubated with HIV-1_{MB} chronically infected CEM cells (10^4) in 96-well flat-bottomed half-area plates (Costar) in 100 μl culture medium. Peptide and fusion proteins at various concentrations in 10 μl culture medium were incubated with the cell mixtures at 37°C for 24 hours. Multinucleated syncytia were estimated with microscopic examination. Both M41 and M41-P did not show cytotoxicity at the concentrations tested and shown in FIG. 8.

Inhibition of HIV-1 induced cell-cell fusion activity was carried out in the presence of 10 nM DP178 and various concentrations of M41Δ178 or M41-PΔ178 as indicated in FIG. 9. There was no observable syncytia in the presence of 10 nM DP178. No peptide or fusion protein was added in the control samples.

8.1.4. ELISA ANALYSIS OF DP178 BINDING TO THE LEUCINE ZIPPER MOTIF OF GP41

The amino acid sequence of DP178 used is: YTSLIHSLIEESQNQQEKNEQELLELDKWASLWNWF. For enzyme linked immunoassay (ELISA), M41Δ178 or M41-PΔ178 (5 μg/ml) in 0.1M $NaHCO_3$, pH 8.6, were coated on 96 wells

Linbro ELISA plates (Flow Lab, Inc.) overnight. Each well was washed three times with distilled water then blocked with 3% bovine serum albumin (BSA) for 2 hours. After blocking, peptides with 0.5% BSA in TBST (40 mM Tris-HCl pH7.5, 150 mM NaCl, 0.05% Tween 20) were added to the ELISA plates and incubated at room temperature for 1 hour. After washing three times with TBST, Fab-d was added at a concentration of 10 ng/ml with 0.5% BSA in TBST. The plates were washed three times with TBST after incubation at room temperature for 1 hour. Horse radish peroxidase (HRP) conjugated goat antihuman Fab antiserum at a 2000 fold dilution in TBST with 0.5% BSA was added to each well and incubated at room temperature for 45 minutes. The plates were then washed four times with TBST. The peroxidase substrate o-phenylene diamine (2.5 mg/ml) and 0.15% H_2O_2 were added to develop the color. The reaction was stopped with an equal volume of 4.5 N H_2SO_4 after incubation at room temperature for 10 minutes. The optical density of the stopped reaction mixture was measured with a micro plate reader (Molecular Design) at 490 nm. Results are shown in FIG. 10.

8.2. RESULTS

8.2.1. THE EXPRESSION AND CHARACTERIZATION OF THE ECTODOMAIN OF GP41

As a step toward understanding the roles of the two helical regions in gp41 structure and function, the ectodomain of gp41 was expressed as a maltose binding fusion protein (M41) (Fig. 7). The fusogenic peptide sequence at the N-terminal of gp41 was omitted from this recombinant protein and its derivatives to improve solubility. The maltose binding protein facilitated purification of the fusion proteins under relatively mild, non-denaturing conditions. Because

the M41 soluble recombinant gp41 was not glycosylated, lacked several regions of the transmembrane protein (i.e., the fusion peptide, the membrane spanning, and the cytoplasmic domains), and was expressed in the absence of gp120, it was not expected to precisely reflect the structure of native gp41 on HIV-1 virions. Nevertheless, purified M41 folded in a manner that preserved certain discontinuous epitopes as evidenced by reactivity with human monoclonal antibodies, 98-6, 126-6, and 50-69, previously shown to bind conformational epitopes on native gp41 expressed in eukaryotic cells (Xu et al., 1991, J. Virol. 65: 4832-4838; Chen, 1994, J. Virol. 68:2002-2010). Thus, at least certain regions of native gp41 defined by these antibodies appear to be reproduced in the recombinant fusion protein M41. Furthermore, M41 reacted with a human recombinant Fab (Fab-d) that recognizes a conformational epitope on gp41 and binds HIV-1 virions as well as HIV-1 infected cells but not uninfected cells as analyzed by FACS. Deletion of either helix motif, i.e., DP107 or DP178, of the M41 fusion protein eliminated reactivity with Fab-d. These results indicate that both helical regions, separated by 60 amino acids in the primary sequence, are required to maintain the Fab-d epitope.

8.2.2. ANTI-HIV ACTIVITY OF THE RECOMBINANT ECTODOMAIN OF GP41

The wild type M41 fusion protein was tested for anti-HIV-1 activity. As explained, supra, synthetic peptides corresponding to the leucine zipper (DP107) and the C-terminal putative helix (DP178) show potent anti-HIV activity. Despite inclusion of both these regions, the recombinant M41 protein did not affect

HIV-1 induced membrane fusion at concentrations as high as 50 μM (Table XII, below).

TABLE XII

DISRUPTION OF THE LEUCINE ZIPPER OF GP41 FREES THE ANTI-HIV MOTIF

	DP107	DP178	M41	M41-P	M41-PΔ178
Cell fusion (IC_{90})	1 μM	1 nM	>50 μM	83 nM	>50 μM
Fab-D binding (k_D)	-	-	$3.5x10^{-9}$	$2.5x10^{-8}$	-
HIV infectivity (IC_{90})	1 μM	80 nM	>16 μM	66 nM	>8 μM

1 The affinity constants of Fab-d binding to the fusion proteins were determined using a protocol described by B. Friguet et al., 1985, J. Immunol. Method. 77:305-319.

- = No detectable binding of Fab-d to the fusion proteins.

Antiviral Infectivity Assays. 20 μl of serially diluted virus stock was incubated for 60 minutes at ambient temperature with 20 μl of the indicated concentration of purified recombinant fusion protein in RPMI 1640 containing 10% fetal bovine serum and antibiotics in a 96-well microtiter plate. 20 μl of CEM4 cells at 6 x 10^5 cells/ml were added to each well, and cultures were incubated at 37°C in a humidified CO_2 incubator. Cells were cultured for 9 days by the addition of fresh medium every 2 to 30 days. On days 5, 7, and 9 postinfection, supernatant samples were assayed for reverse transcriptase (RT) activity, as described below, to monitor viral replication. The 50% tissue culture infectious dose ($TCID_{50}$) was calculated for each condition according to the formula of Reed & Muench, 1937, Am. J. Hyg. 27:493-497. RT activity was determined by a modification of the published methods of Goff et al., 1981, J. Virol. 38:239-248 and Willey et al., 1988, J. Virol. 62:139-147 as described in Chen et al., 1993, AIDS Res. Human Retroviruses 9:1079-1086.

Surprisingly, a single amino acid substitution, proline in place of isoleucine in the middle of the leucine zipper motif, yielded a fusion protein (M41-P)

which did exhibit antiviral activity (Table XII and Fig. 8). As seen in Table XII, M41-P blocked syncytia formation by 90% at approximately 85 nM and neutralized HIV-1_{IIIB} infection by 90% at approximately 70 nM concentrations. The anti-HIV-1 activity of M41-P appeared to be mediated by the C-terminal helical sequence since deletion of that region from M41-P yielded an inactive fusion protein, M41-PΔ178 (Table XII). That interpretation was reinforced by experiments demonstrating that a truncated fusion protein lacking the DP178 sequence, M41Δ178, abrogated the potent anti-fusion activity of the DP178 peptide in a concentration-dependent manner (FIG. 9). The same truncated fusion protein containing the proline mutation disrupting the leucine zipper, M41-PΔ178, was not active in similar competition experiments (FIG. 9). The results indicate that the DP178 peptide associates with a second site on gp41 whose interactive structure is dependent on a wild type leucine zipper sequence. A similar interaction may occur within the wild type fusion protein, M41, and act to form an intramolecular clasp which sequesters the DP178 region, making it unavailable for anti-viral activity.

A specific association between these two domains is also indicated by other human monoclonal Fab-d studies. For example, Fab-d failed to bind either the DP178 peptide or the fusion protein M41Δ178, but its epitope was reconstituted by simply mixing these two reagents together (FIG. 10). Again, the proline mutation in the leucine zipper domain of the fusion protein, M41-PΔ178, failed to reconstitute the epitope in similar mixing experiments.

9. EXAMPLE: METHOD FOR COMPUTER-ASSISTED IDENTIFICATION OF DP-107-LIKE AND DP-178-LIKE SEQUENCES

A number of known coiled-coil sequences have been well described in the literature and contain heptad repeat positioning for each amino acid. Coiled-coil nomenclature labels each of seven amino acids of a heptad repeat A through G, with amino acids A and D tending to be hydrophobic positions. Amino acids E and G tend to be charged. These four positions (A, D, E, and G) form the amphipathic backbone structure of a monomeric alpha-helix. The backbones of two or more amphipathic helices interact with each other to form di-, tri-, tetrameric, etc., coiled-coil structures. In order to begin to design computer search motifs, a series of well characterized coiled coils were chosen including yeast transcription factor GCN4, Influenza Virus hemagglutinin loop 36, and human proto-oncogenes c-Myc, c-Fos, and c-Jun. For each peptide sequence, a strict homology for the A and D positions, and a list of the amino acids which could be excluded for the B, C, E, F, and G positions (because they are not observed in these positions) was determined. Motifs were tailored to the DP-107 and DP-178 sequences by deducing the most likely possibilities for heptad positioning of the amino acids of HIV-1 Bru DP-107, which is known to have coiled-coil structure, and HIV-1 Bru DP-178, which is still structurally undefined. The analysis of each of the sequences is contained in FIG. 12. For example, the motif for GCN4 was designed as follows:

1. The only amino acids (using standard single letter amino acid codes) found in the A or D positions of GCN4 were [LMNV].
2. All amino acids were found at B, C, E, F, and G positions except {CFGIMPTW}.

3. The PESEARCH motif would, therefore, be written as follows:

[LMNV]-{CFGIMPTW}(2)-[LMNV]-{CFGIMPTW}(3)-
[LMNV]-{CFGIMPTW}(2)-[LMNV]-{CFGIMPTW}(3)-
[LMNV]-{CFGIMPTW}(2)-[LMNV]-{CFGIMPTW}(3)-
[LMNV]-{CFGIMPTW}(2)-[LMNV]-{CFGIMPTW}(3)

Translating or reading the motif: "at the first A position either L, M, N, or V must occur; at positions B and C (the next two positions) accept everything except C, F, G, I, M, P, T, or W; at the D position either L, M, N, or V must occur; at positions E, F, and G (the next 3 positions) accept everything except C, F, G, I, M, P, T, or W." This statement is contained four times in a 28-mer motif and five times in a 35-mer motif. The basic motif key then would be: [LMNV]-{CFGIMPTW}. The motif keys for the remaining well described coiled-coil sequences are summarized in FIG. 12.

The motif design for DP-107 and DP-178 was slightly different than the 28-mer model sequences described above due to the fact that heptad repeat positions are not defined and the peptides are both longer than 28 residues. FIG. 13 illustrates several possible sequence alignments for both DP-107 and DP-178 and also includes motif designs based on 28^{mer}, 35^{mer}, and full-length peptides. Notice that only slight differences occur in the motifs as the peptides are lengthened. Generally, lengthening the base peptide results in a less stringent motif. This is very useful in broadening the possibilities for identifying DP-107-or DP-178-like primary amino acid sequences referred to in this document as "hits".

In addition to making highly specific motifs for each type peptide sequence to be searched, it is also possible to make "hybrid" motifs. These motifs are

made by "crossing" two or more very stringent motifs to make a new search algorithm which will find not only both "parent" motif sequences but also any peptide sequences which have similarities to one, the other, or both "parents". For example, in Table 3 the "parent" sequence of GCN4 is crossed with each of the possible "parent" motifs of DP-107. Now the hybrid motif must contain all of the amino acids found in the A and D positions of both parents, and exclude all of the amino acids not found in either parent at the other positions. The resulting hybrid from crossing GCN4 or [LMNV]{CFGIMPTW} and DP-107 (28-mer with the first L in the D position) or [ILQT]{CDFIMPST}, is [ILMNQTV]{CFIMPT}. Notice that now only two basic hybrid motifs exist which cover both framing possibilities, as well as all peptide lengths of the parent DP-107 molecule. FIG. 15 represents the hybridizations of GCN4 with DP-178. FIG. 16 represents the hybridizations of DP-107 and DP-178. It is important to keep in mind that the represented motifs, both parent and hybrid, are motif keys and not the depiction of the full-length motif needed to actually do the computer search.

Hybridizations can be performed on any combination of two or more motifs. Table 5 summarizes several three-motif hybridizations including GCN4, DP-107 (both frames), and DP-178 (also both frames). Notice that the resulting motifs are now becoming much more similar to each other. In fact, the first and third hybrid motifs are actually subsets of the second and fourth hybrid motifs respectively. This means that the first and third hybrid motifs are slightly more stringent than the second and fourth. It should also be noted that with only minor changes in these four motifs, or by hybridizing them, a single motif could be obtained

which would find all of the sequences. However, it should be remembered that stringency is also reduced. Finally, the most broad-spectra and least-stringent hybrid motif is described in FIG. 18 which summarizes the hybridization of GCN4, DP-107 (both frames), DP-178 (both frames), c-Fos, c-Jun, c-Myc, and Flu loop 36.

A special set of motifs was designed based on the fact that DP-178 is located only approximately ten amino acids upstream of the transmembrane spanning region of gp41 and just C-terminal to a proline which separates DP-107 and DP-178. It has postulated that DP-178 may be an amphipathic helix when membrane associated, and that the proline might aid in the initiation of the helix formation. The same arrangement was observed in Respiratory Syncytial Virus; however, the DP-178-like region in this virus also had a leucine zipper just C-terminal to the proline. Therefore, designed N-terminal proline-leucine zipper motifs were designed to analyze whether any other viruses might contain this same pattern. The motifs are summarized in FIG. 19.

The PC/Gene protein database contains 5879 viral amino acid sequences (library file PVIRUSES; CD-ROM release 11.0). Of these, 1092 are viral envelope or glycoprotein sequences (library file PVIRUSE1). Tables V through X contain lists of protein sequence names and motif hit locations for all the motifs searched.

10. EXAMPLE: COMPUTER-ASSISTED IDENTIFICATION OF DP-107 AND DP-178-LIKE SEQUENCES IN HUMAN IMMUNODEFICIENCY VIRUS

FIG. 20 represents search results for HIV-1 BRU isolate gp41 (PC/Gene protein sequence PENV_HV1BR). Notice that the hybrid motif which crosses DP-107 and

DP-178 (named 107x178x4; the same motif as found in FIG. 16 found three hits including amino acids 550-599, 636-688, and 796-823. These areas include DP-107 plus eight N-terminal and four C-terminal amino acids; DP-178 plus seven N-terminal and ten C-terminal amino acids; and an area inside the transmembrane region (cytoplasmic). FIG. 20 also contains the results obtained from searching with the motif named ALLMOTI5, for which the key is found in FIG. 17 ({CDGHP}{CFP}x5). This motif also found three hits including DP-107 (amino acids 510-599), DP-178 (615-717), and a cytoplasmic region (772-841). These hits overlap the hits found by the motif 107x178x4 with considerable additional sequences on both the amino and carboxy termini. This is not surprising in that 107x178x4 is a subset of the ALLMOTI5 hybrid motif. Importantly, even though the stringency of ALLMOTI5 is considerably less than 107x178x4, it still selectively identifies the DP-107 and DP-178 regions of gp41 shown to contain sequences for inhibitory peptides of HIV-1. The results of these two motif searches are summarized in Table V under the PC/Gene protein sequence name PENV HV1BR. The proline-leucine zipper motifs also gave several hits in HIV-1 BRU including 503-525 which is at the very C-terminus of gp120, just upstream of the cleavage site (P7LZIPC and P12LZIPC); and 735-768 in the cytoplasmic domain of gp41 (P23LZIPC). These results are found in Tables VIII, IX, and X under the same sequence name as mentioned above. Notice that the only area of HIV-1 BRU which is predicted by the Lupas algorithm to contain a coiled-coil region, is from amino acids 635-670. This begins eight amino acids N-terminal to the start and ends eight amino acids N-terminal to the end of DP-178. DP-107, despite the fact that it is a known coiled coil, is

not predicted to contain a coiled-coil region using the Lupas method.

11. EXAMPLE: COMPUTER-ASSISTED IDENTIFICATION OF DP-107-LIKE AND DP-178-LIKE SEQUENCES IN HUMAN RESPIRATORY SYNCYTIAL VIRUS

FIG. 21 represents search results for Human Respiratory Syncytial Virus (RSV; Strain A2) fusion glycoprotein F1 (PC/Gene protein sequence name PVGLF_HRSVA). Motif 107x178x4 finds three hits including amino acids 152-202, 213-243, and 488-515. The arrangement of these hits is similar to what is found in HIV-1 except that the motif finds two regions with similarities to DP-178, one just downstream of what would be called the DP-107 region or amino acids 213-243, and one just upstream of the transmembrane region (also similar to DP-178) or amino acids 488-515. Motif ALLMOTI5 also finds three areas including amino acids 116-202, 267-302, and 506-549. The proline-leucine zipper motifs also gave several hits including amino acids 205-221 and 265-287 (P1LZIPC 265-280, P12LZIPC), and 484-513 (P7LZIPC and P12LZIPC 484-506, P23LZIPC). Notice that the PLZIP motifs also identify regions which share location similarities with DP-178 of HIV-1.

12. EXAMPLE: COMPUTER-ASSISTED IDENTIFICATION OF DP-107-LIKE AND DP-178-LIKE SEQUENCES IN SIMIAN IMMUNODEFICIENCY VIRUS

Motif hits for Simian immunodeficiency Virus gp41 (AGM3 isolate; PC/Gene protein sequence name PENV_SIVAG) are shown in FIG. 22. Motif 107x178x4 finds three hits including amino acids 566-593, 597-624, and 703-730. The first two hits only have three amino acids between them and could probably be combined into one hit from 566-624 which would

represent a DP-107-like hit. Amino acids 703 to 730 would then represent a DP-178-like hit. ALLMOTI5 also finds three hits including amino acids 556-628 (DP-107-like), 651-699 (DP-178-like), and 808-852 which represents the transmembrane spanning region. SIV also has one region from 655-692 with a high propensity to form a coiled coil as predicted by the Lupas algorithm. Both 107x178x4 and ALLMOTI5 motifs find the same region. SIV does not have any PLZIP motif hits in gp41.

13. EXAMPLE: COMPUTER-ASSISTED IDENTIFICATION OF DP-107-LIKE AND DP-178 LIKE SEQUENCES IN CANINE DISTEMPER VIRUS

Canine Distemper Virus (strain Onderstepoort) fusion glycoprotein F1 (PC/Gene Protein sequence name PVGLF_CDVO) has regions similar to Human RSV which are predicted to be DP-107-like and DP-178-like (FIG. 23). Motif 107x178x4 highlights one area just C-terminal to the fusion peptide at amino acids 252-293. Amino acids 252-286 are also predicted to be coiled coil using the Lupas algorithm. Almost 100 amino acids C-terminal to the first region is a DP-178-like area at residues 340-367. ALLMOTI5 highlights three areas of interest including: amino acids 228-297, which completely overlaps both the Lupas prediction and the DP-107-like 107x178x4 hit; residues 340-381, which overlaps the second 107x178x4 hit; and amino acids 568-602, which is DP178-like in that it is located just N-terminal to the transmembrane region. It also overlaps another region (residues 570-602) predicted by the Lupas method to have a high propensity to form a coiled coil. Several PLZIP motifs successfully identified areas of interest including P6 and P12LZIPC which highlight residues 336-357 and 336-361 respectively; P1 and P12LZIPC which find residues 398-

414; and P12 and P23LZIPC which find residues 562-589 and 562-592 respectively.

14. EXAMPLE: COMPUTER-ASSISTED IDENTIFICATION OF DP-107-LIKE AND DP-178-LIKE SEQUENCES IN NEWCASTLE DISEASE VIRUS

FIG. 24 shows the motif hits found in Newcastle Disease Virus (strain Australia-Victoria/32; PC Gene protein sequence name PVGLF_NDVA). Motif 107x178x4 finds two areas including a DP-107-like hit at amino acids 151-178 and a DP-178-like hit at residues 426-512. ALLMOTI5 finds three areas including residues 117-182, 231-272, and 426-512. The hits from 426-512 include a region which is predicted by the Lupas method to have a high coiled-coil propensity (460-503). The PLZIP motifs identify only one region of interest at amino acids 273-289 (P1 and 12LZIPC).

15. EXAMPLE: COMPUTER-ASSISTED IDENTIFICATION OF DP-107-LIKE AND DP-178-LIKE SEQUENCES IN HUMAN PARAINFLUENZA VIRUS

Both motifs 107x178x4 and ALLMOTI5 exhibit DP-107-like hits in the same region, 115-182 and 117-182 respectively, of Human Parainfluenza Virus (strain NIH 47885; PC/Gene protein sequence name PVGLF_p13H4; (FIG. 25). In addition, the two motifs have a DP-178-like hit just slightly C-terminal at amino acids 207-241. Both motifs also have DP-178-like hits nearer the transmembrane region including amino acids 457-497 and 462-512 respectively. Several PLZIP motif hits are also observed including 283-303 (P5LZIPC), 283-310 (P12LZIPC), 453-474 (P6LZIPC), and 453-481 (P23LZIPC). The Lupas algorithm predicts that amino acids 122-176 have a propensity to form a coiled-coil.

16. EXAMPLE: COMPUTER-ASSISTED IDENTIFICATION OF DP-107-LIKE AND DP-178-LIKE SEQUENCES OF INFLUENZA A VIRUS

FIG. 26 illustrates the Lupas prediction for a coiled coil in Influenza A Virus (strain A/Aichi/2/68) at residues 379-436, as well as the motif hits for 107x178x4 at amino acids 387-453, and for ALLMOTI5 at residues 380-456. Residues 383-471 (38-125 of HA2) were shown by Carr and Kim to be an extended coiled coil when under acidic pH (Carr and Kim, 1993, Cell 73: 823-832). The Lupas algorithyan predicts a coiled-coil at residues 379-436. All three methods successfully predicted the region shown to actually have coiled-coil structure; however, ALLMOTI5 predicted the greatest portion of the 88 residue stretch.

17. EXAMPLE: RSV ANTIVIRAL COMPOUNDS

In the Example presented herein, respiratory syncytial virus (RSV) peptide sequences identified by utilizing the computer-assisted coiled-coil peptide sequence searches described in Example 9, above, are shown to encode peptide domains that exhibit structural similarity to actual, known coiled-coil peptides, and are, additionally found to exhibit antiviral activity.

17.1 MATERIALS AND METHODS

Structural analyses consisted of circular dichroism (CD) studies, which were conducted according to the methods described in the Applicants' co-pending U.S. Patent Application Ser. No 08/073,028.

Anti-RSV antiviral activity was assayed as described in Pringle, C.R. et al., 1985, J. Medical Vir. 17:377-386.

A 48 amino acid RSV F2 peptide and a 53 amino acid RSV T67 peptide are utilized which span sequences that were identified via the computer assisted peptide sequence search strategies described in Example 9, above. See FIG. 21 for the exact position of these sequences and for the motifs utilized.

17.2 RESULTS

35-mer oligopeptides were synthesized which constituted portions of the 48 amino acid RSV F2 peptide sequence (FIG. 27) and portions of the 53 amino acid RSV T67 peptide sequence (FIG. 28). The oligopeptides were assayed, via CD analysis, for structural similarity to known coiled-coil structures, and for anti-RSV activity. As shown in FIGS. 27 and 28, a number of these oligopeptides exhibited substantial coiled-coil structural similarity and/or antiviral activity.

Thus, the computer assisted searches described, herein, in Example 9, for example, successfully identified viral peptide domains that represent highly promising anti-RSV antiviral compounds.

18. EXAMPLE: HPF3 ANTIVIRAL COMPOUNDS

In the Example presented herein, human parainfluenza virus 3 (HPF3) peptide sequences identified by utilizing the computer-assisted coiled-coil peptide sequence searches described in Example 9, above, are shown to encode peptide domains that exhibit structural similarity to actual, known coiled-coil peptides, and are, additionally found to exhibit antiviral activity.

18.1 MATERIALS AND METHODS

Structural analyses consisted of circular dichroism (CD) studies, which were conducted according

to the methods described in the Applicants' co-pending U.S. Patent Application Ser. No 08/073,028.

Anti-HPF3 antiviral activity was assayed as described in Pringle, C.R. et al., 1985, J. Medical Vir. 17:377-386.

A 56 amino acid and 70 amino acid HPF3 peptide are utilized which span sequences that were identified via the computer assisted peptide sequence search strategies described in Example 9, above. See FIG. 25 for the exact positions of these sequences and for the motifs utilized.

18.2 RESULTS

35-mer oligopeptides were synthesized which constituted portions of the 56 amino acid HPF3 peptide sequence (FIG. 29) and portions of the 70 amino acid HPF3 peptide sequence (FIG. 30). The oligopeptides were assayed, via CD analysis, for structural similarity to known coiled-coil structures, and for anti-HPF3 activity. As shown in FIGS. 29 and 30, a number of these oligopeptides exhibited substantial coiled-coil structural similarity and/or antiviral activity.

Thus, the computer assisted searches described, herein, in Example 9, for example, successfully identified viral peptide domains that represent highly promising anti-HPF3 antiviral compounds.

The present invention is not to be limited in scope by the specific embodiments described which are intended as single illustrations of individual aspects of the invention, and functionally equivalent methods and components are within the scope of the invention. Indeed, various modifications of the invention, in addition to those shown and described herein will become apparent to those skilled in the art from the

foregoing description and accompanying drawings. Such modifications are intended to fall within the scope of the appended claims.

WHAT IS CLAIMED IS:

1. A peptide having an amino acid sequence corresponding to an α-helix region of an extracellular domain of a viral envelope protein, which interacts with and binds to a second α-helix region of the viral envelope protein containing a leucine-zipper domain having a coiled-coil structure.

2. The peptide of Claim 1 wherein the peptide is recognized by a computer-assisted peptide sequence search utilizing an ALLMOTI5, 107x178x4 motif, or a PLZIP motif.

3. The peptide of Claim 1 in which the enveloped virus is a retrovirus.

4. The peptide of Claim 3 in which the retrovirus is a human retrovirus.

5. The peptide of Claim 4 in which the human retrovirus is HIV-1 or HIV-2.

6. The peptide of Claim 4 in which the human retrovirus is HTLV-I or HTLV-II

7. The peptide of Claim 1 in which the enveloped virus is a non-human retrovirus.

8. The peptide of Claim 6 in which the non-human retrovirus is bovine leukosis virus, feline sarcoma virus, feline leukemia virus, simian immunodeficiency virus, simian sarcoma virus, and sheep progress pneumonia virus.

9. The peptide of Claim 1 in which the enveloped virus is a non-retroviral virus.

10. The peptide of Claim 9 in which the virus is respiratory syncytial virus, influenza virus, parainfluenza virus, canine distemper virus, or newcastle disease virus.

11. A peptide having a formula selected from the group consisting of:

X-YTS-Z
X-YTSL-Z
X-YTSLI-Z
X-YTSLIH-Z
X-YTSLIHS-Z
X-YTSLIHSL-Z
X-YTSLIHSLI-Z
X-YTSLIHSLIE-Z
X-YTSLIHSLIEE-Z
X-YTSLIHSLIEES-Z
X-YTSLIHSLIEESQ-Z
X-YTSLIHSLIEESQN-Z
X-YTSLIHSLIEESQNQ-Z
X-YTSLIHSLIEESQNQQ-Z
X-YTSLIHSLIEESQNQQE-Z
X-YTSLIHSLIEESQNQQEK-Z
X-YTSLIHSLIEESQNQQEKN-Z
X-YTSLIHSLIEESQNQQEKNE-Z
X-YTSLIHSLIEESQNQQEKNEQ-Z
X-YTSLIHSLIEESQNQQEKNEQE-Z
X-YTSLIHSLIEESQNQQEKNEQEL-Z
X-YTSLIHSLIEESQNQQEKNEQELL-Z
X-YTSLIHSLIEESQNQQEKNEQELLE-Z
X-YTSLIHSLIEESQNQQEKNEQELLEL-Z
X-YTSLIHSLIEESQNQQEKNEQELLELD-Z
X-YTSLIHSLIEESQNQQEKNEQELLELDK-Z
X-YTSLIHSLIEESQNQQEKNEQELLELDKW-Z
X-YTSLIHSLIEESQNQQEKNEQELLELDKWA-Z
X-YTSLIHSLIEESQNQQEKNEQELLELDKWAS-Z
X-YTSLIHSLIEESQNQQEKNEQELLELDKWASL-Z
X-YTSLIHSLIEESQNQQEKNEQELLELDKWASLW-Z
X-YTSLIHSLIEESQNQQEKNEQELLELDKWASLWN-Z
X-YTSLIHSLIEESQNQQEKNEQELLELDKWASLWNW-Z and
X-YTSLIHSLIEESQNQQEKNEQELLELDKWASLWNWF-Z (SEQ ID:1), or

X-NWF-Z
X-WNWF-Z
X-LWNWF-Z
X-SLWNWF-Z
X-ASLWNWF-Z
X-WASLWNWF-Z
X-KWASLWNWF-Z
X-DKWASLWNWF-Z
X-LDKWASLWNWF-Z
X-ELDKWASLWNWF-Z
X-LELDKWASLWNWF-Z
X-LLELDKWASLWNWF-Z
X-ELLELDKWASLWNWF-Z
X-QELLELDKWASLWNWF-Z
X-EQELLELDKWASLWNWF-Z
X-NEQELLELDKWASLWNWF-Z
X-KNEQELLELDKWASLWNWF-Z
X-EKNEQELLELDKWASLWNWF-Z
X-QEKNEQELLELDKWASLWNWF-Z
X-QQEKNEQELLELDKWASLWNWF-Z
X-NQQEKNEQELLELDKWASLWNWF-Z
X-QNQQEKNEQELLELDKWASLWNWF-Z
X-SQNQQEKNEQELLELDKWASLWNWF-Z
X-ESQNQQEKNEQELLELDKWASLWNWF-Z
X-EESQNQQEKNEQELLELDKWASLWNWF-Z
X-IEESQNQQEKNEQELLELDKWASLWNWF-Z
X-LIEESQNQQEKNEQELLELDKWASLWNWF-Z
X-SLIEESQNQQEKNEQELLELDKWASLWNWF-Z
X-HSLIEESQNQQEKNEQELLELDKWASLWNWF-Z
X-IHSLIEESQNQQEKNEQELLELDKWASLWNWF-Z
X-LIHSLIEESQNQQEKNEQELLELDKWASLWNWF-Z
X-SLIHSLIEESQNQQEKNEQELLELDKWASLWNWF-Z
and X-TSLIHSLIEESQNQQEKNEQELLELDKWASLWNWF-Z

in which:

amino acid residues are presented by the single-letter code;

X comprises an amino group, an acetyl group, a 9-fluorenylmethoxy-carbonyl group, a hydrophobic group, or a macromolecule carrier group;

Z comprises a carboxyl group, an amido group, a hydrophobic group, or a macromolecular carrier group.

12. A peptide having a formula selected from the group consisting of:

X-LEA-Z
X-LEAN-Z
X-LEANI-Z
X-LEANIS-Z
X-LEANISQ-Z
X-LEANISQS-Z
X-LEANISQSL-Z
X-LEANISQSLE-Z
X-LEANISQSLEQ-Z
X-LEANISQSLEQA-Z
X-LEANISQSLEQAQ-Z
X-LEANISQSLEQAQI-Z
X-LEANISQSLEQAQIQ-Z
X-LEANISQSLEQAQIQQ-Z
X-LEANISQSLEQAQIQQE-Z
X-LEANISQSLEQAQIQQEK-Z
X-LEANISQSLEQAQIQQEKN-Z
X-LEANISQSLEQAQIQQEKNM-Z
X-LEANISQSLEQAQIQQEKNMY-Z
X-LEANISQSLEQAQIQQEKNMYE-Z
X-LEANISQSLEQAQIQQEKNMYEL-Z
X-LEANISQSLEQAQIQQEKNMYELQ-Z
X-LEANISQSLEQAQIQQEKNMYELQK-Z
X-LEANISQSLEQAQIQQEKNMYELQKL-Z
X-LEANISQSLEQAQIQQEKNMYELQKLN-Z
X-LEANISQSLEQAQIQQEKNMYELQKLNS-Z
X-LEANISQSLEQAQIQQEKNMYELQKLNSW-Z
X-LEANISQSLEQAQIQQEKNMYELQKLNSWD-Z
X-LEANISQSLEQAQIQQEKNMYELQKLNSWDV-Z
X-LEANISQSLEQAQIQQEKNMYELQKLNSWDVF-Z
X-LEANISQSLEQAQIQQEKNMYELQKLNSWDVFT-Z
X-LEANISQSLEQAQIQQEKNMYELQKLNSWDVFTN-Z
X-LEANISQSLEQAQIQQEKNMYELQKLNSWDVFTNW-Z and
X-LEANISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z (SEQ ID:7), or

X-NWL-Z
X-TNWL-Z
X-FTNWL-Z
X-VFTNWL-Z
X-DVFTNWL-Z
X-WDVFTNWL-Z
X-SWDVFTNWL-Z
X-NSWDVFTNWL-Z
X-LNSWDVFTNWL-Z
X-KLNSWDVFTNWL-Z
X-QKLNSWDVFTNWL-Z
X-LQKLNSWDVFTNWL-Z
X-ELQKLNSWDVFTNWL-Z
X-YELQKLNSWDVFTNWL-Z
X-MYELQKLNSWDVFTNWL-Z
X-NMYELQKLNSWDVFTNWL-Z
X-KNMYELQKLNSWDVFTNWL-Z
X-EKNMYELQKLNSWDVFTNWL-Z
X-QEKNMYELQKLNSWDVFTNWL-Z

X-QQEKNMYELQKLNSWDVFTNWL-Z
X-IQQEKNMYELQKLNSWDVFTNWL-Z
X-QIQQEKNMYELQKLNSWDVFTNWL-Z
X-AQIQQEKNMYELQKLNSWDVFTNWL-Z
X-QAQIQQEKNMYELQKLNSWDVFTNWL-Z
X-EQAQIQQEKNMYELQKLNSWDVFTNWL-Z
X-LEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
X-SLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
X-QKSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
X-SQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
X-ISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
X-NISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
X-ANISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
and X-EANISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z

in which:

amino acid residues are presented by the single-letter code;

X comprises an amino group, an acetyl group, a 9-fluoromethyoxymethyl-carbonyl group, a hydrophobic group, or a macromolecule carrier group;

Z comprises a carboxyl group, an amido group, a hydrophobic group, or a macromolecular carrier group.

13. A peptide having a formula selected from the group consisting of:

X-YTS-Z
X-YTSV-Z
X-YTSVI-Z
X-YTSVIT-Z
X-YTSVITI-Z
X-YTSVITIE-Z
X-YTSVITIEL-Z
X-YTSVITIELS-Z
X-YTSVITIELSN-Z
X-YTSVITIELSNI-Z
X-YTSVITIELSNIK-Z
X-YTSVITIELSNIKE-Z
X-YTSVITIELSNIKEN-Z
X-YTSVITIELSNIKENK-Z
X-YTSVITIELSNIKENKC-Z
X-YTSVITIELSNIKENKCN-Z
X-YTSVITIELSNIKENKCNG-Z
X-YTSVITIELSNIKENKCNGT-Z
X-YTSVITIELSNIKENKCNGTD-Z

X-YTSVITIELSNIKENKCNGTDA-Z
X-YTSVITIELSNIKENKCNGTDAK-Z
X-YTSVITIELSNIKENKCNGTDAKV-Z
X-YTSVITIELSNIKENKCNGTDAKVK-Z
X-YTSVITIELSNIKENKCNGTDAKVKL-Z
X-YTSVITIELSNIKENKCNGTDAKVKLI-Z
X-YTSVITIELSNIKENKCNGTDAKVKLIK-Z
X-YTSVITIELSNIKENKCNGTDAKVKLIKQ-Z
X-YTSVITIELSNIKENKCNGTDAKVKLIKQE-Z
X-YTSVITIELSNIKENKCNGTDAKVKLIKQEL-Z
X-YTSVITIELSNIKENKCNGTDAKVKLIKQELD-Z
X-YTSVITIELSNIKENKCNGTDAKVKLIKQELDK-Z
X-YTSVITIELSNIKENKCNGTDAKVKLIKQELDKY-Z
X-YTSVITIELSNIKENKCNGTDAKVKLIKQELDKYK-Z
X-YTSVITIELSNIKENKCNGTDAKVKLIKQELDKYKN-Z
X-YTSVITIELSNIKENKCNGTDAKVKLIKQELDKYKNA-Z
X-YTSVITIELSNIKENKCNGTDAKVKLIKQELDKYKNAV-Z
X-YTSVITIELSNIKENKCNGTDAKVKLIKQELDKYKNAVT-Z
X-YTSVITIELSNIKENKCNGTDAKVKLIKQELDKYKNAVTE-Z
X-YTSVITIELSNIKENKCNGTDAKVKLIKQELDKYKNAVTEL-Z
X-YTSVITIELSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQ-Z
X-YTSVITIELSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQL-Z
X-YTSVITIELSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLL-Z
X-YTSVITIELSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLM-Z
X-YTSVITIELSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQ-Z
X-YTSVITIELSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQS-Z and
X-YTSVITIELSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z, or

X-QST-Z
X-MQST-Z
X-LMQST-Z
X-LLMQST-Z
X-QLLMQST-Z
X-LQLLMQST-Z
X-ELQLLMQST-Z
X-TELQLLMQST-Z
X-VTELQLLMQST-Z
X-AVTELQLLMQST-Z
X-NAVTELQLLMQST-Z
X-KNAVTELQLLMQST-Z
X-YKNAVTELQLLMQST-Z
X-KYKNAVTELQLLMQST-Z
X-DKYKNAVTELQLLMQST-Z
X-LDKYKNAVTELQLLMQST-Z
X-ELDKYKNAVTELQLLMQST-Z
X-QELDKYKNAVTELQLLMQST-Z
X-KQELDKYKNAVTELQLLMQST-Z
X-IKQELDKYKNAVTELQLLMQST-Z
X-LIKQELDKYKNAVTELQLLMQST-Z
X-KLIKQELDKYKNAVTELQLLMQST-Z
X-VKLIKQELDKYKNAVTELQLLMQST-Z
X-KVKLIKQELDKYKNAVTELQLLMQST-Z
X-AKVKLIKQELDKYKNAVTELQLLMQST-Z
X-DAKVKLIKQELDKYKNAVTELQLLMQST-Z

X-TDAKVKLIKQELDKYKNAVTELQLLMQST-Z
X-GTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
X-NGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
X-CNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
X-KCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
X-NKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
X-ENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
X-KENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
X-IKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
X-NIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
X-SNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
X-LSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
X-ELSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
X-IELSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
X-TIELSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
X-ITIELSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
X-VITIELSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
X-SVITIELSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
X-TSVITIELSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z

in which:

amino acid residues are presented by the single-letter code;

X comprises an amino group, an acetyl group, a 9-fluoromethyoxymethyl-carbonyl group, a hydrophobic group, or a macromolecule carrier group;

Z comprises a carboxyl group, an amido group, a hydrophobic group, or a macromolecular carrier group.

14. A peptide having a formula selected from the group consisting of:

X-FYD-Z
X-FYDP-Z
X-FYDPL-Z
X-FYDPLV-Z
X-FYDPLVF-Z
X-FYDPLVFP-Z
X-FYDPLVFPS-Z
X-FYDPLVFPSD-Z
X-FYDPLVFPSDE-Z
X-FYDPLVFPSDEF-Z
X-FYDPLVFPSDEFD-Z
X-FYDPLVFPSDEFDA-Z
X-FYDPLVFPSDEFDAS-Z
X-FYDPLVFPSDEFDASI-Z

X-FYDPLVFPSDEFDASIS-Z
X-FYDPLVFPSDEFDASISQ-Z
X-FYDPLVFPSDEFDASISQV-Z
X-FYDPLVFPSDEFDASISQVN-Z
X-FYDPLVFPSDEFDASISQVNE-Z
X-FYDPLVFPSDEFDASISQVNEK-Z
X-FYDPLVFPSDEFDASISQVNEKI-Z
X-FYDPLVFPSDEFDASISQVNEKIN-Z
X-FYDPLVFPSDEFDASISQVNEKINQ-Z
X-FYDPLVFPSDEFDASISQVNEKINQS-Z
X-FYDPLVFPSDEFDASISQVNEKINQSL-Z
X-FYDPLVFPSDEFDASISQVNEKINQSLA-Z
X-FYDPLVFPSDEFDASISQVNEKINQSLAF-Z
X-FYDPLVFPSDEFDASISQVNEKINQSLAFI-Z
X-FYDPLVFPSDEFDASISQVNEKINQSLAFIR-Z
X-FYDPLVFPSDEFDASISQVNEKINQSLAFIRK-Z
X-FYDPLVFPSDEFDASISQVNEKINQSLAFIRKS-Z
X-FYDPLVFPSDEFDASISQVNEKINQSLAFIRKSD-Z
X-FYDPLVFPSDEFDASISQVNEKINQSLAFIRKSDE-Z
X-FYDPLVFPSDEFDASISQVNEKINQSLAFIRKSDEL-Z
X-FYDPLVFPSDEFDASISQVNEKINQSLAFIRKSDELL-Z, or

X-DELL-Z
X-SDELL-Z
X-KSDELL-Z
X-RKSDELL-Z
X-IRKSDELL-Z
X-FIRKSDELL-Z
X-AFIRKSDELL-Z
X-LAFIRKSDELL-Z
X-SLAFIRKSDELL-Z
X-QSLAFIRKSDELL-Z
X-NQSLAFIRKSDELL-Z
X-INQSLAFIRKSDELL-Z
X-KINQSLAFIRKSDELL-Z
X-EKINQSLAFIRKSDELL-Z
X-NEKINQSLAFIRKSDELL-Z
X-VNEKINQSLAFIRKSDELL-Z
X-QVNEKINQSLAFIRKSDELL-Z
X-SQVNEKINQSLAFIRKSDELL-Z
X-ISQVNEKINQSLAFIRKSDELL-Z
X-SISQVNEKINQSLAFIRKSDELL-Z
X-ASISQVNEKINQSLAFIRKSDELL-Z
X-DASISQVNEKINQSLAFIRKSDELL-Z
X-FDASISQVNEKINQSLAFIRKSDELL-Z
X-EFDASISQVNEKINQSLAFIRKSDELL-Z
X-DEFDASISQVNEKINQSLAFIRKSDELL-Z
X-SDEFDASISQVNEKINQSLAFIRKSDELL-Z
X-PSDEFDASISQVNEKINQSLAFIRKSDELL-Z
X-FPSDEFDASISQVNEKINQSLAFIRKSDELL-Z
X-VFPSDEFDASISQVNEKINQSLAFIRKSDELL-Z
X-LVFPSDEFDASISQVNEKINQSLAFIRKSDELL-Z
X-PLVFPSDEFDASISQVNEKINQSLAFIRKSDELL-Z
X-DPLVFPSDEFDASISQVNEKINQSLAFIRKSDELL-Z

X-YDPLVFPSDEFDASISQVNEKINQSLAFIRKSDELL-Z

in which:
amino acid residues are presented by the single-letter code;
X comprises an amino group, an acetyl group, a 9-fluoromethyoxymethyl-carbonyl group, a hydrophobic group, or a macromolecule carrier group;
Z comprises a carboxyl group, an amido group, a hydrophobic group, or a macromolecular carrier group.

15. A peptide having a formula selected from the group consisting of:
X-ITL-Z
X-ITLN-Z
X-ITLNN-Z
X-ITLNNS-Z
X-ITLNNSV-Z
X-ITLNNSVA-Z
X-ITLNNSVAL-Z
X-ITLNNSVALD-Z
X-ITLNNSVALDP-Z
X-ITLNNSVALDPI-Z
X-ITLNNSVALDPID-Z
X-ITLNNSVALDPIDI-Z
X-ITLNNSVALDPIDIS-Z
X-ITLNNSVALDPIDISI-Z
X-ITLNNSVALDPIDISIE-Z
X-ITLNNSVALDPIDISIEL-Z
X-ITLNNSVALDPIDISIELN-Z
X-ITLNNSVALDPIDISIELNK-Z
X-ITLNNSVALDPIDISIELNKA-Z
X-ITLNNSVALDPIDISIELNKAK-Z
X-ITLNNSVALDPIDISIELNKAKS-Z
X-ITLNNSVALDPIDISIELNKAKSD-Z
X-ITLNNSVALDPIDISIELNKAKSDL-Z
X-ITLNNSVALDPIDISIELNKAKSDLE-Z
X-ITLNNSVALDPIDISIELNKAKSDLEE-Z
X-ITLNNSVALDPIDISIELNKAKSDLEES-Z
X-ITLNNSVALDPIDISIELNKAKSDLEESK-Z
X-ITLNNSVALDPIDISIELNKAKSDLEESKE-Z
X-ITLNNSVALDPIDISIELNKAKSDLEESKEW-Z
X-ITLNNSVALDPIDISIELNKAKSDLEESKEWI-Z
X-ITLNNSVALDPIDISIELNKAKSDLEESKEWIR-Z

X-ITLNNSVALDPIDISIELNKAKSDLEESKEWIRR-Z
X-ITLNNSVALDPIDISIELNKAKSDLEESKEWIRRS-Z, or

X-RRS-Z
X-IRRS-Z
X-WIRRS-Z
X-EWIRRS-Z
X-KEWIRRS-Z
X-SKEWIRRS-Z
X-ESKEWIRRS-Z
X-EESKEWIRRS-Z
X-LEESKEWIRRS-Z
X-DLEESKEWIRRS-Z
X-SDLEESKEWIRRS-Z
X-KSDLEESKEWIRRS-Z
X-AKSDLEESKEWIRRS-Z
X-KAKSDLEESKEWIRRS-Z
X-NKAKSDLEESKEWIRRS-Z
X-LNKAKSDLEESKEWIRRS-Z
X-ELNKAKSDLEESKEWIRRS-Z
X-IELNKAKSDLEESKEWIRRS-Z
X-SIELNKAKSDLEESKEWIRRS-Z
X-ISIELNKAKSDLEESKEWIRRS-Z
X-DISIELNKAKSDLEESKEWIRRS-Z
X-IDISIELNKAKSDLEESKEWIRRS-Z
X-PIDISIELNKAKSDLEESKEWIRRS-Z
X-DPIDISIELNKAKSDLEESKEWIRRS-Z
X-LDPIDISIELNKAKSDLEESKEWIRRS-Z
X-ALDPIDISIELNKAKSDLEESKEWIRRS-Z
X-VALDPIDISIELNKAKSDLEESKEWIRRS-Z
X-SVALDPIDISIELNKAKSDLEESKEWIRRS-Z
X-NSVALDPIDISIELNKAKSDLEESKEWIRRS-Z
X-NNSVALDPIDISIELNKAKSDLEESKEWIRRS-Z
X-LNNSVALDPIDISIELNKAKSDLEESKEWIRRS-Z
X-TLNNSVALDPIDISIELNKAKSDLEESKEWIRRS-Z

in which:

amino acid residues are presented by the single-letter code;

X comprises an amino group, an acetyl group, a 9-fluoromethyoxymethyl-carbonyl group, a hydrophobic group, or a macromolecule carrier group;

Z comprises a carboxyl group, an amido group, a hydrophobic group, or a macromolecular carrier group.

16. A peptide having a formula selected from the group consisting of:

X-ALG-Z
X-ALGV-Z
X-ALGVA-Z
X-ALGVAT-Z
X-ALGVATS-Z
X-ALGVATSA-Z
X-ALGVATSAQ-Z
X-ALGVATSAQI-Z
X-ALGVATSAQIT-Z
X-ALGVATSAQITA-Z
X-ALGVATSAQITAA-Z
X-ALGVATSAQITAAV-Z
X-ALGVATSAQITAAVA-Z
X-ALGVATSAQITAAVAL-Z
X-ALGVATSAQITAAVALV-Z
X-ALGVATSAQITAAVALVE-Z
X-ALGVATSAQITAAVALVEA-Z
X-ALGVATSAQITAAVALVEAK-Z
X-ALGVATSAQITAAVALVEAKQ-Z
X-ALGVATSAQITAAVALVEAKQA-Z
X-ALGVATSAQITAAVALVEAKQAR-Z
X-ALGVATSAQITAAVALVEAKQARS-Z
X-ALGVATSAQITAAVALVEAKQARSD-Z
X-ALGVATSAQITAAVALVEAKQARSDI-Z
X-ALGVATSAQITAAVALVEAKQARSDIE-Z
X-ALGVATSAQITAAVALVEAKQARSDIEK-Z
X-ALGVATSAQITAAVALVEAKQARSDIEKL-Z
X-ALGVATSAQITAAVALVEAKQARSDIEKLK-Z
X-ALGVATSAQITAAVALVEAKQARSDIEKLKE-Z
X-ALGVATSAQITAAVALVEAKQARSDIEKLKEA-Z
X-ALGVATSAQITAAVALVEAKQARSDIEKLKEAI-Z
X-ALGVATSAQITAAVALVEAKQARSDIEKLKEAIR-Z
X-ALGVATSAQITAAVALVEAKQARSDIEKLKEAIRD-Z, or

X-IRD-Z
X-AIRD-Z
X-EAIRD-Z
X-KEAIRD-Z
X-LKEAIRD-Z
X-KLKEAIRD-Z
X-EKLKEAIRD-Z
X-IEKLKEAIRD-Z
X-DIEKLKEAIRD-Z
X-SDIEKLKEAIRD-Z
X-RSDIEKLKEAIRD-Z
X-ARSDIEKLKEAIRD-Z
X-QARSDIEKLKEAIRD-Z
X-KQARSDIEKLKEAIRD-Z
X-AKQARSDIEKLKEAIRD-Z
X-EAKQARSDIEKLKEAIRD-Z
X-VEAKQARSDIEKLKEAIRD-Z

X-LVEAKQARSDIEKLKEAIRD-Z
X-ALVEAKQARSDIEKLKEAIRD-Z
X-VALVEAKQARSDIEKLKEAIRD-Z
X-AVALVEAKQARSDIEKLKEAIRD-Z
X-AAVALVEAKQARSDIEKLKEAIRD-Z
X-TAAVALVEAKQARSDIEKLKEAIRD-Z
X-ITAAVALVEAKQARSDIEKLKEAIRD-Z
X-QITAAVALVEAKQARSDIEKLKEAIRD-Z
X-AQITAAVALVEAKQARSDIEKLKEAIRD-Z
X-SAQITAAVALVEAKQARSDIEKLKEAIRD-Z
X-TSAQITAAVALVEAKQARSDIEKLKEAIRD-Z
X-ATSAQITAAVALVEAKQARSDIEKLKEAIRD-Z
X-VATSAQITAAVALVEAKQARSDIEKLKEAIRD-Z
X-GVATSAQITAAVALVEAKQARSDIEKLKEAIRD-Z
X-LGVATSAQITAAVALVEAKQARSDIEKLKEAIRD-Z

in which:

amino acid residues are presented by the single-letter code;

X comprises an amino group, an acetyl group, a 9-fluoromethyoxymethyl-carbonyl group, a hydrophobic group, or a macromolecule carrier group;

Z comprises a carboxyl group, an amido group, a hydrophobic group, or a macromolecular carrier group.

17. The peptide of Claim 11, 12, 13, 14, 15 or 16 wherein X is a hydrophobic group.

18. The peptide of Claim 17 wherein the hydrophobic group X is carbobenzoxyl, dansyl, or t-butyloxycarbonyl.

19. The peptide of Claim 11, 12, 13, 14, 15 or 16 wherein Z is a hydrophobic group.

20. The peptide of Claim 19 wherein the hydrophobic group Z is t-butyloxycarbonyl.

21. The peptide of Claim 11, 12, 13, 14, 15 or 16 wherein X is a macromolecular carrier group.

22. The peptide of Claim 21 wherein the macromolecular carrier group is a lipid-fatty acid conjugate, a polyethylene glycol, or a carbohydrate moiety.

23. The peptide of Claim 11, 12, 13, 14, 15 or 16 wherein Z is a macromolecular carrier group.

24. The peptide of Claim 23 wherein the macromolecular carrier group Z is a lipid-fatty acid conjugate, a polyethylene glycol, or a carbohydrate moiety.

25. The peptide of Claim 11, 12, 13, 14, 15 or 16 wherein at least one bond linking adjacent amino acid residues is a non-peptide bond.

26. The peptide of Claim 25 wherein the non-peptide bond is an inino, ester, hydrazine, semicarbazide, or azo bond.

27. The peptide of Claim 11, 12, 13, 14, 15 or 16 wherein at least one amino acid residue is in a D-isomer configuration.

28. The peptide of Claim 11, 12, 13, 14, 15 or 16 further comprising at least one amino acid insertion.

29. The peptide of Claim 11, 12, 13, 14, 15 or 16 wherein the amino acid insertion is between 1 and 15 amino acid residues.

30. The peptide of Claim 11, 12, 13, 14, 15 or 16 having at least one less amino acid residue, wherein the amino acid residue(s) represents an amino acid deletion, and wherein the peptide comprises at least three amino acid residues.

31. The peptide of Claim 11, 12, 13, 14, 15 or 16 further comprising at least one amino acid substitution wherein a first amino acid residue is substituted for a second, different amino acid residue.

32. The peptide of Claim 31 wherein the amino acid substitution is a conserved substitution.

33. The peptide of Claim 31 wherein the amino acid substitution is a non-conserved substitution.

34. A method for the inhibition of transmission of an enveloped virus to a cell, comprising contacting the cell with an effective concentration of the peptide of Claim 1 for an effective period of time so that no infection of the cell by the virus occurs.

35. A method for neutralizing an enveloped virus in a host, comprising administering to the host an effective concentration of the peptide of Claim 1 so that the host raises an immune response sufficient to neutralize the virus, and viral infection of uninfected cells in the host is inhibited.

36. A method for neutralizing an enveloped virus in a host, comprising administering to the host an effective concentration of an antibody raised against the peptide of Claim 1 so that viral infection of uninfected cells in the host is inhibited.

37. A method for the detection of an enveloped virus comprising:

contacting a viral isolate with an effective concentration of the peptide of Claim 1 for an effective amount of time so that viral infectivity is inhibited; and

assaying the viral isolate for viral enzyme activity.

38. A method for the inhibition of transmission of an HIV retrovirus to a cell, comprising contacting the cell with an effective concentration of the peptide of Claim 11 or 12 for an effective period of time so that no infection of the cell by the retrovirus occurs.

39. A method for neutralizing an HIV retrovirus in a host, comprising administering to the host an effective concentration of the peptide of Claim 11 or 12 so that the host raises an immune response sufficient to neutralize the HIV retrovirus, and HIV infection of uninfected cells in the host is inhibited.

40. A method for neutralizing an HIV retrovirus in a host, comprising administering to the host an effective concentration of an antibody raised against the peptide of Claim 11 or 12 so that HIV infection of uninfected cells in the host is inhibited.

41. A method for the detection of HIV, comprising:

contacting a viral isolate with an effective concentration of the peptide of Claim 11 or 12 for an effective amount of time so that HIV viral infectivity is inhibited; and

assaying the viral isolate for retroviral enzyme activity.

42. A method for the inhibition of transmission of a respiratory syncytial virus to a cell, comprising contacting the cell with an effective concentration of the peptide of Claim 13 or 14 for an effective period of time so that no infection of the cell by the virus occurs.

43. A method for neutralizing a respiratory syncytial virus in a host, comprising administering to the host an effective concentration of the peptide of Claim 13 or 14 so that the host raises an immune response sufficient to neutralize the virus, and respiratory syncytial virus infection of uninfected cells in the host is inhibited.

44. A method for neutralizing a respiratory syncytial virus in a host comprising administering to the host an effective concentration of an antibody raised against the peptide of Claim 13 or 14 so that respiratory syncytial virus infection of uninfected cells in the host is inhibited.

45. A method for the detection of respiratory syncytial virus comprising:

contacting a viral isolate with an effective concentration of the peptide of Claim 13 or 14 for an effective amount of time so that respiratory syncytial viral infectivity is inhibited; and

assaying the viral isolate for respiratory syncytial virus enzyme activity.

46. A method for the inhibition of transmission of a parainfluenza virus to a cell comprising,

contacting the cell with an effective concentration of the peptide of Claim 15 or 16 for an effective period of time so that no infection of the cell by the virus occurs.

47. A method for neutralizing a parainfluenza virus in a host, comprising administering to the host an effective concentration of the peptide of Claim 15 or 16 so that the host raises an immune response sufficient to neutralize the virus, and parainfluenza infection of uninfected cells in the host is inhibited.

48. A method for neutralizing a parainfluenza virus in a host comprising administering to the host an effective concentration of an antibody raised against the peptide of Claim 15 or 16 so that parainfluenza infection of uninfected cells in the host is inhibited.

49. A method for the detection of parainfluenza virus comprising:

contacting a viral isolate with an effective concentration of the peptide of Claim 15 or 16 for an effective amount of time so that parainfluenza viral infectivity is inhibited; and

assaying the viral isolate for parainfluenza virus enzyme activity.

HIV1LAI (DP-178; SEQ ID:1) YTSLIHSLIEESQNQQEKNEQELLELDKWASLWNWF

HIV1SF2 (DP-185; SEQ ID:3) YTNTIYNLLEESQNQQEKNEQELLELDKWASLWNWF

HIV1RF (SEQ ID:4) YTGIIYNLLEESQNQQEKNEQELLELDKWANLWNWF

HIV1MN (SEQ ID:5) YTSLIYSLLEKSQTQQEKNEQELLELDKWASLWNWF

HIV2ROD (SEQ ID:6) LEANISKSLEQAQIQQEKNMYELQKLNSWDIFGNWF

HIV2NIHZ (SEQ ID:7) LEANISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL

DP180 (SEQ ID:2) SSESFTLLEQWNNWKLQLAEQWLEQINEKHYLEDIS

DP118 (SEQ ID:10) QQLLDVVKRQQEMLRLTVWGTKNLQARVTAIEKYLKDQ

DP125 (SEQ ID:8) CGGNNLLRAIEAQQHLLQLTVWGIKQLQARILAVERYLKDQ

DP116 (SEQ ID:9) LQARILAVERYLKDQQQ

FIG. 1

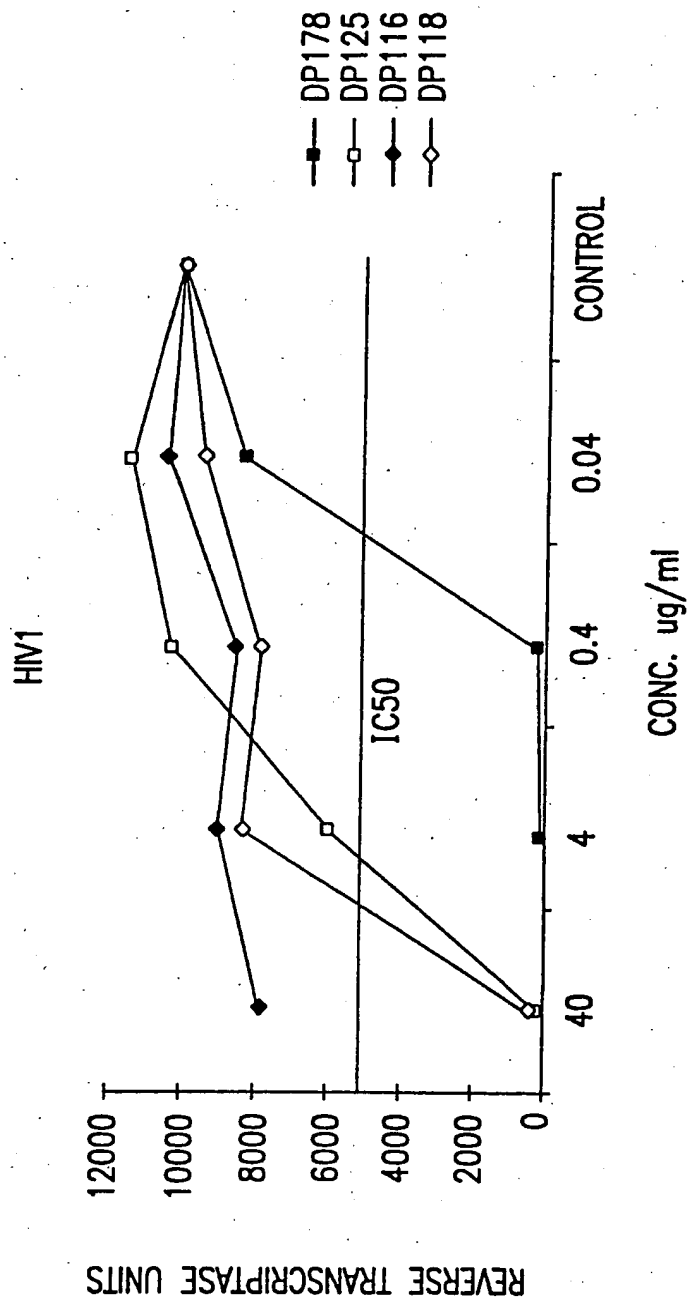
DP178
DP125
DP116
DP118
HIV1
IC50
CONTROL
0.04
0.4
4
40
CONC. ug/ml
12000
10000
8000
6000
4000
2000
0
REVERSE TRANSCRIPTASE UNITS

FIG.2

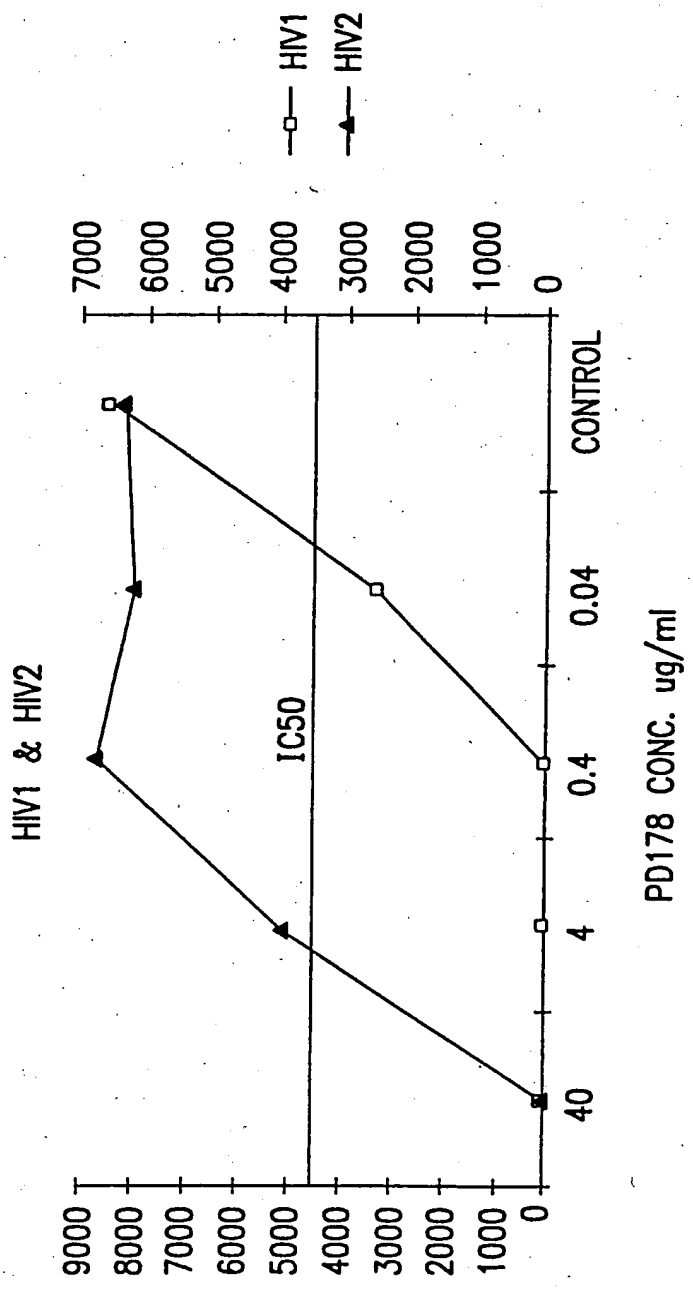
HIV1
HIV2
7000
6000
5000
4000
3000
2000
1000
0
CONTROL
0.04
0.4
4
40
PD178 CONC. ug/ml
HIV1 & HIV2
IC50
9000
8000
7000
6000
5000
4000
3000
2000
1000
0

FIG.3

Number of Syncytia/well: concentration in μg/ml (micrograms/ml)

DP178	10	5	1	0.2	0.1	0.05	0.025	0.0125	Control
Syncytia									
HIV1LAI	0	0	0	0	0	0	0	0	67
HIV1MN	0	0	0	0	0	ND	ND	ND	34
HIV1RF	0	0	0	0	0	ND	ND	ND	65
HIV1SF2	0	0	0	0	0	ND	ND	ND	58

DP125	10	5	1	0.2	0.1	0.05	0.025	0.0125	Control
Syncytia									
HIV1LAI	0	0	54	69	80	75	79	82	67
HIV1MN	0	0	30	36	ND	ND	ND	ND	34
HIV1RF	0	0	67	63	ND	ND	ND	ND	65
HIV1SF2	0	0	9	66	ND	ND	ND	ND	58

DP116	10	5	1	0.2	0.1	0.05	0.025	0.0125	Control
Syncytia									
HIV1LAI	75	ND	ND	ND	ND	ND	ND	ND	67
HIV1MN	35	ND	ND	ND	ND	ND	ND	ND	34
HIV1RF	81	ND	ND	ND	ND	ND	ND	ND	65
HIV1SF2	81	ND	ND	ND	ND	ND	ND	ND	58

FIG.4A

DP180	40	20	10	5	2.5	1.25	0.625	0.3125	Control
Syncytia									
HIV1LAI	50	>45	>45	>45	>45	>45	>45	>45	58

DP185	40	20	10	5	2.5	1.25	0.625	0.3125	Control
Syncytia									
HIV1LAI	0	0	0	0	0	0	0	ND	60

FIG.4B

HIV1

Number of Syncytia/well: concentration in ng/ml (nanograms/ml)

DP178	20	10	5	2.5	1.25	0.625	0.3125	Control
Syncytia HIV1	0	0	0	0	0	14	20	48
DP116	20	10	5	2.5	1.25	0.625	0.3125	Control
Syncytia HIV1	ND	48	ND	ND	ND	ND	ND	ND

HIV2

Number of Syncytia/well: concentration in μg/ml (micrograms/ml)

DP178	20	10	5	2.5	1.25	0.625	0.3125	Control
Syncytia HIV2	50	54	55	57	63	77	78	76
DP116	20	10	5	2.5	1.25	0.625	0.3125	Control
Syncytia HIV2	ND	58	ND	ND	ND	ND	ND	ND

FIG.5

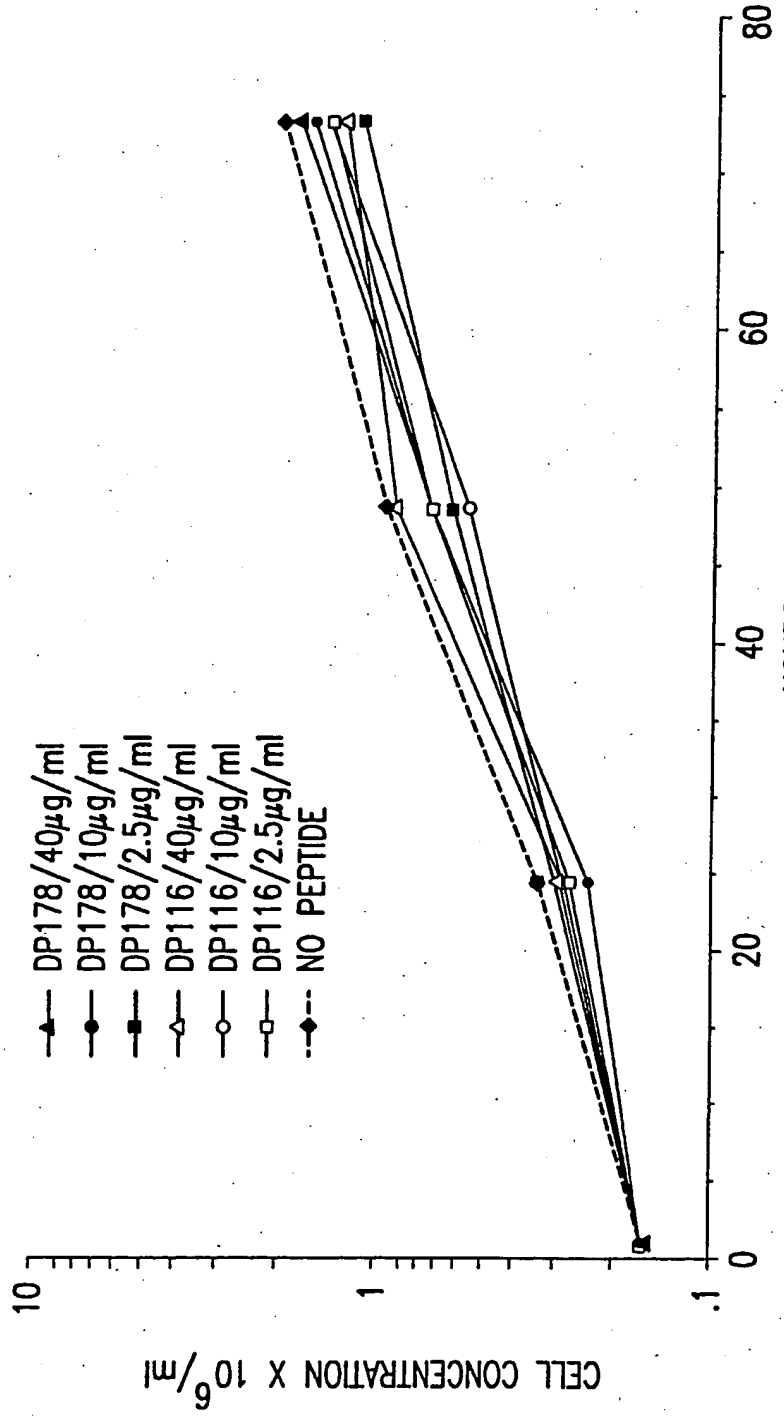
CELL CONCENTRATION X 10^6/ml
10
1
.1
0
20
40
60
80
HOURS
DP178/40μg/ml
DP178/10μg/ml
DP178/2.5μg/ml
DP116/40μg/ml
DP116/10μg/ml
DP116/2.5μg/ml
NO PEPTIDE

FIG.6

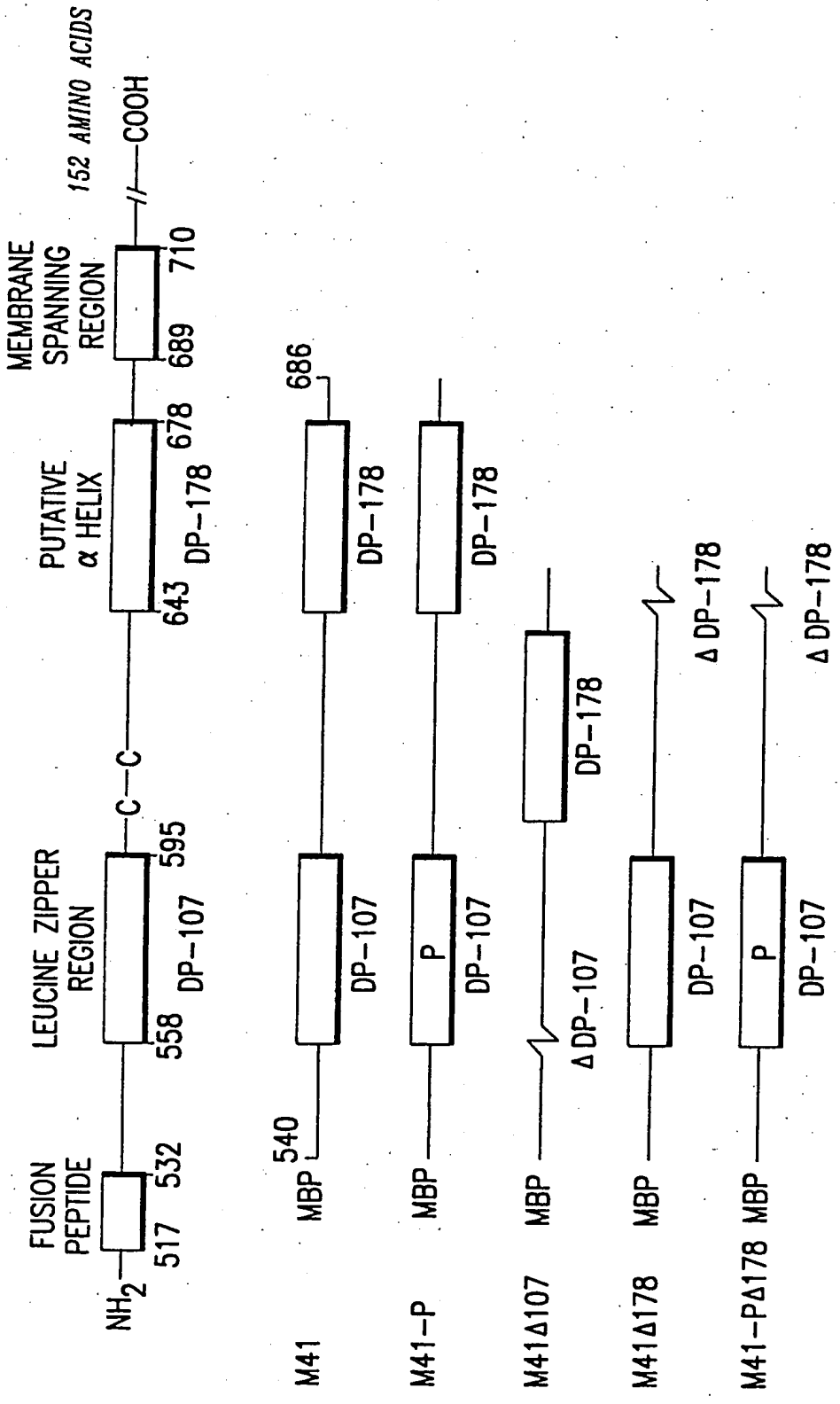
NH2
FUSION PEPTIDE
517
532
LEUCINE ZIPPER REGION
558
595
DP-107
C—C
PUTATIVE α HELIX
643
678
DP-178
MEMBRANE SPANNING REGION
689
710
152 AMINO ACIDS
COOH
M41
MBP
540
DP-107
686
DP-178
M41-P
MBP
P
DP-107
DP-178
M41Δ107
MBP
Δ DP-107
DP-178
M41Δ178
MBP
DP-107
Δ DP-178
M41-PΔ178
MBP
P
DP-107
Δ DP-178

FIG.7

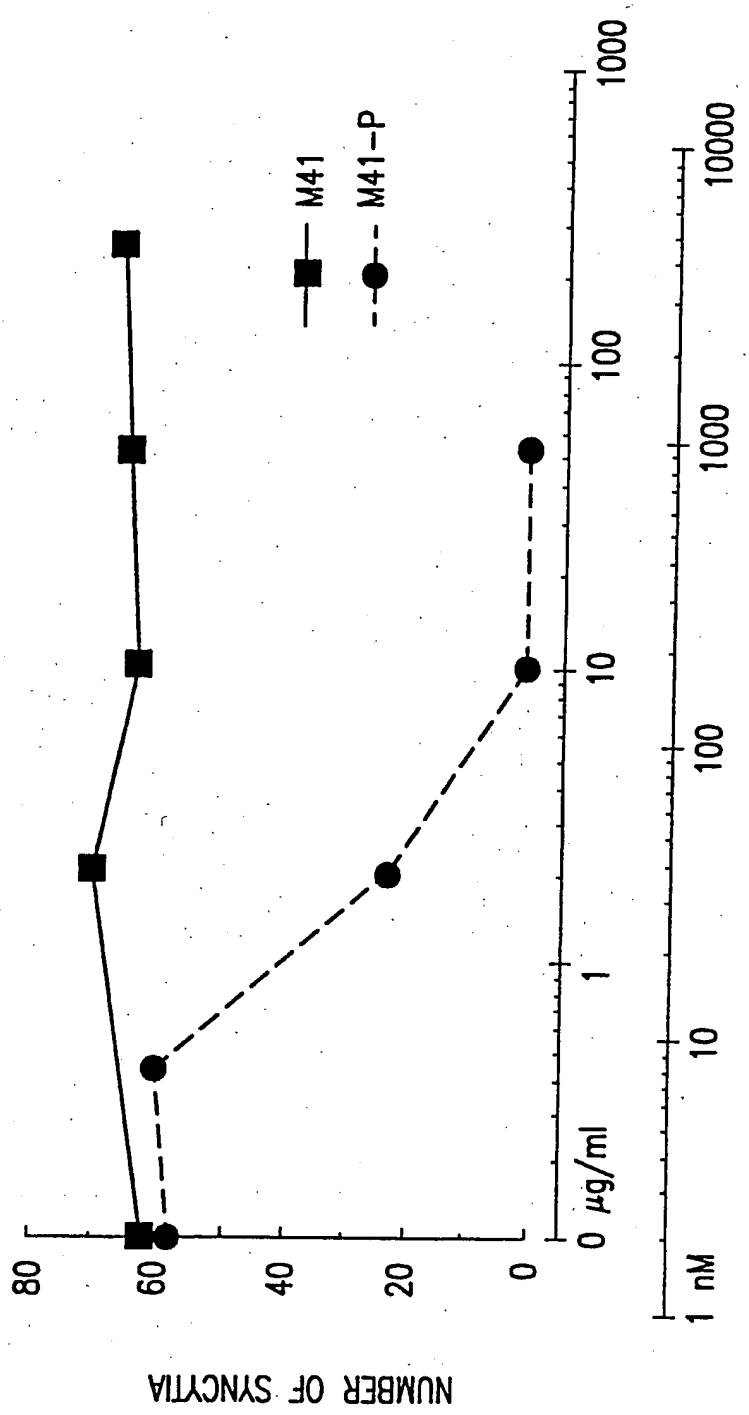
M41
M41-P
NUMBER OF SYNCYTIA
80
60
40
20
0
0 µg/ml
1 nM
1
10
100
1000
10
100
1000
10000

FIG.8

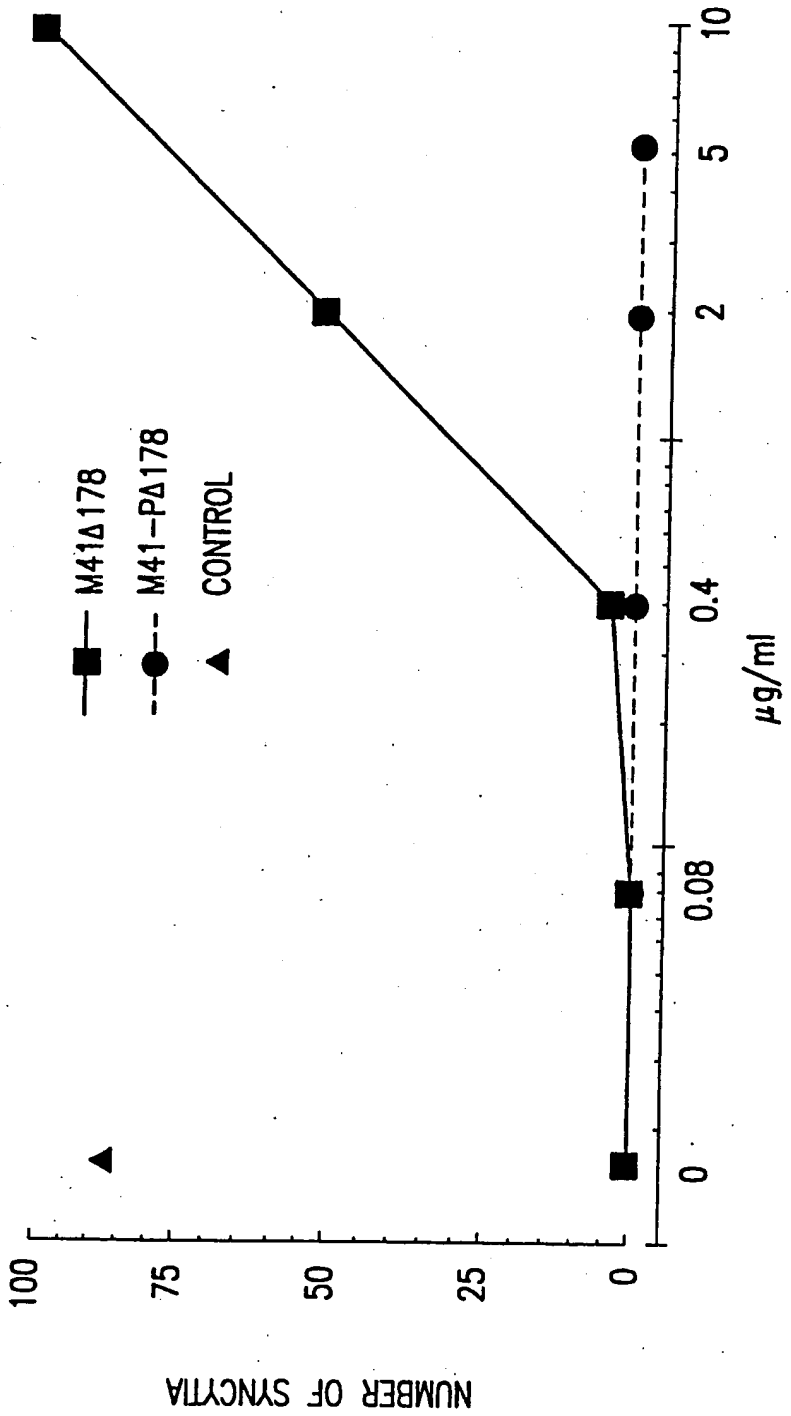
M41Δ178
M41-PΔ178
CONTROL
NUMBER OF SYNCYTIA
100
75
50
25
0
0
0.08
0.4
2
5
10
μg/ml

FIG.9

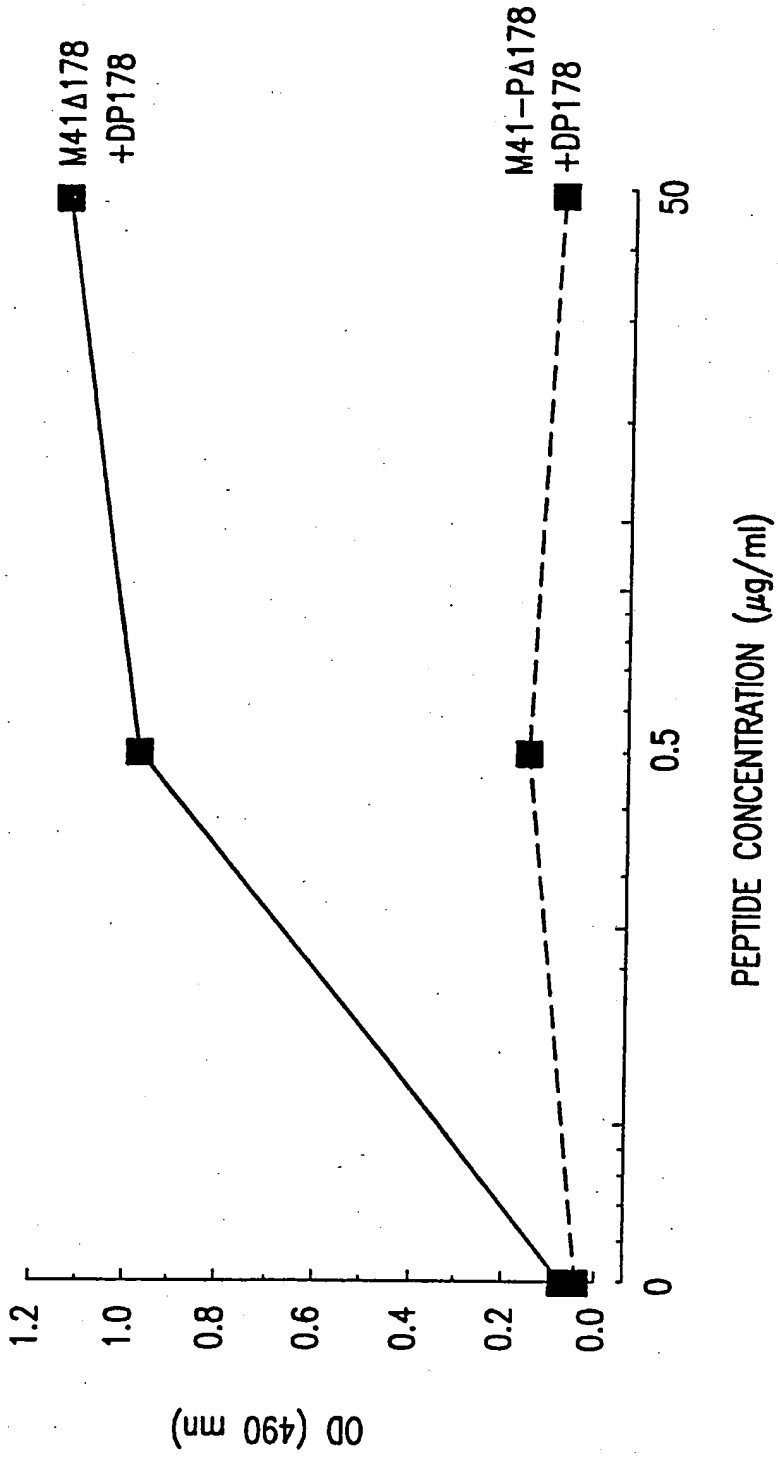
M41Δ178
+DP178
M41-PΔ178
+DP178
1.2
1.0
0.8
0.6
0.4
0.2
0.0
OD (490 mn)
0
0.5
50
PEPTIDE CONCENTRATION (μg/ml)

FIG.10

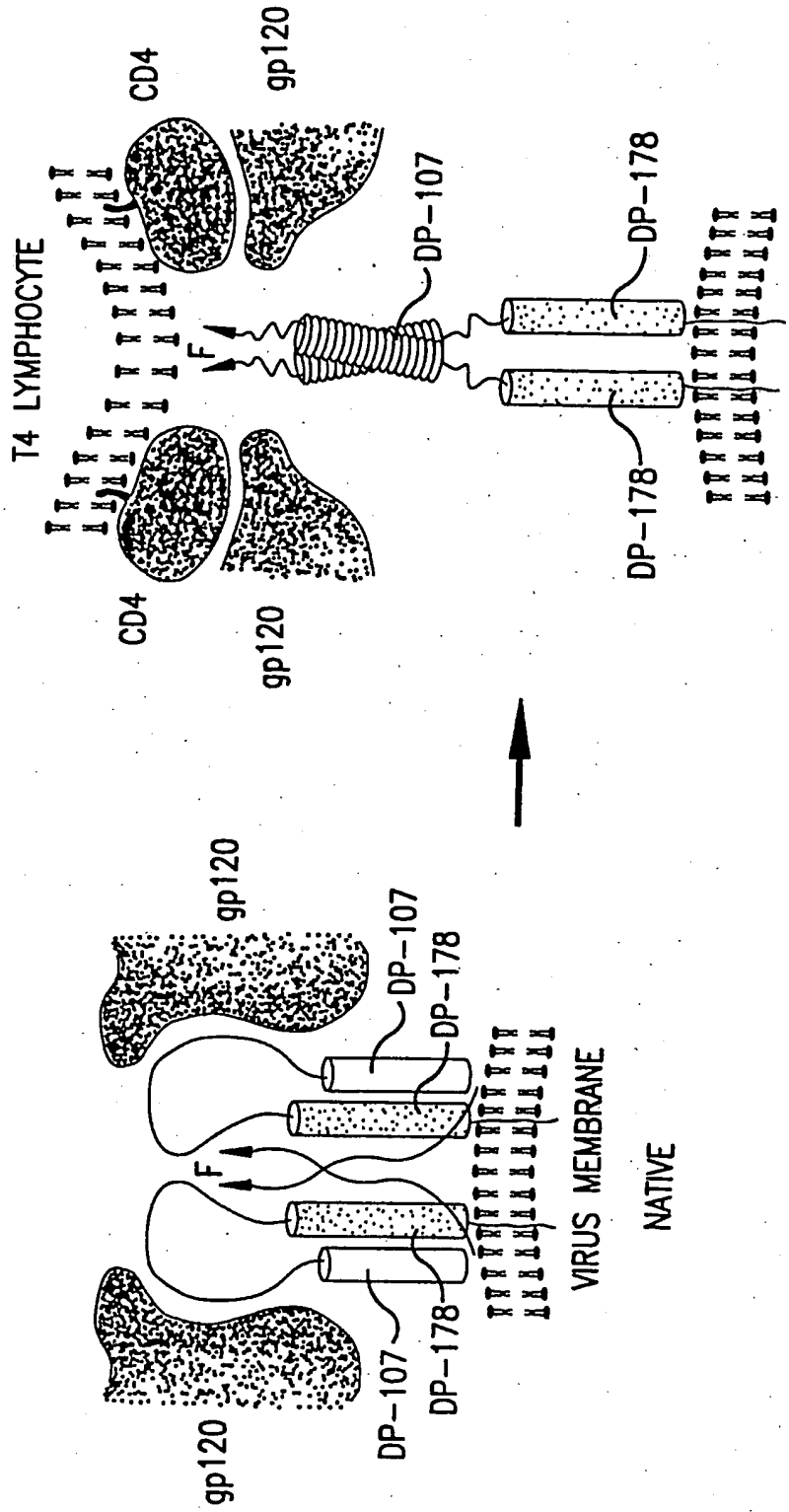
T4 LYMPHOCYTE
CD4
gp120
CD4
gp120
DP-107
DP-178
F
DP-178
FUSOGENIC
gp120
DP-107
DP-178
F
VIRUS MEMBRANE
NATIVE
DP-107
DP-178
gp120

FIG.11A

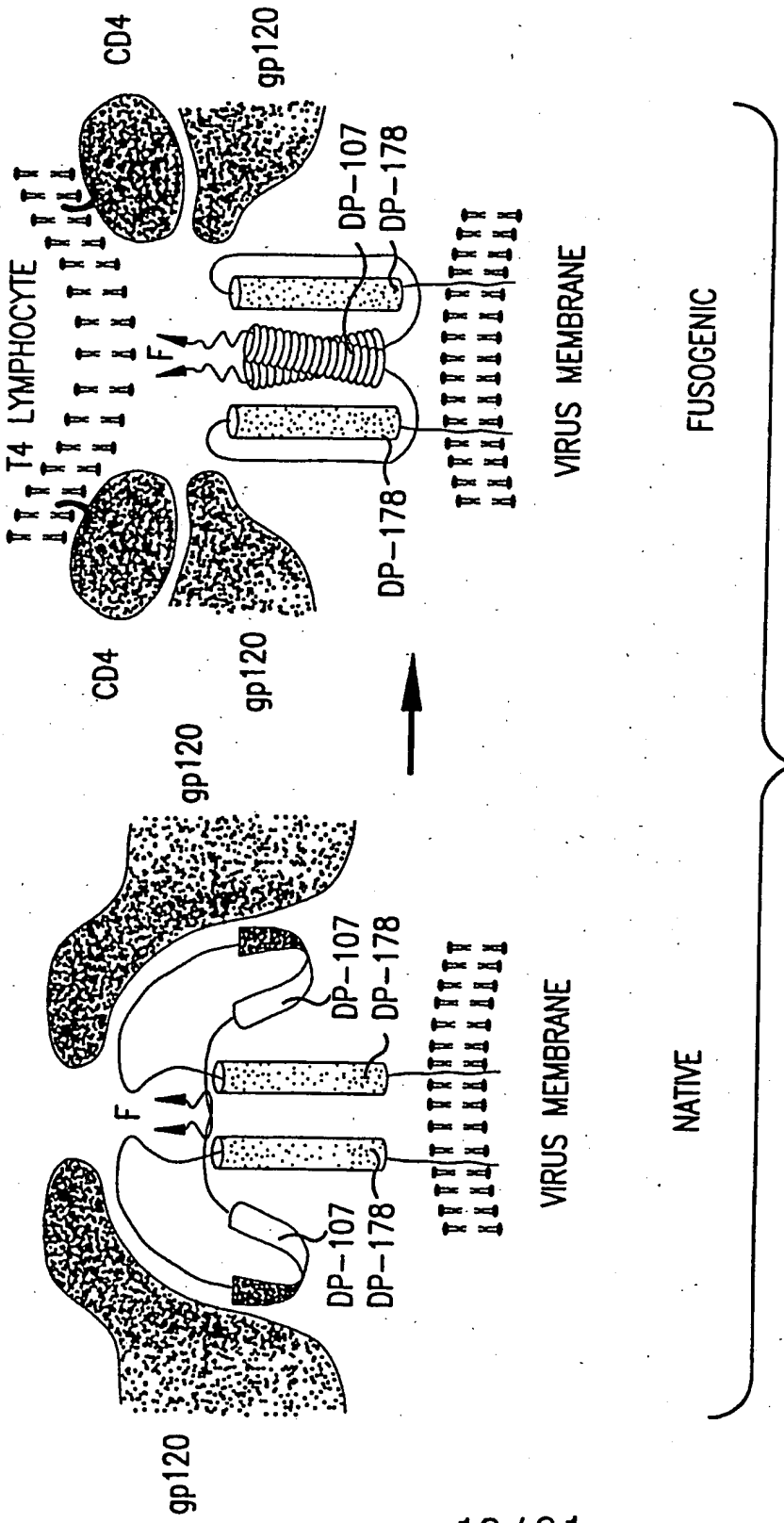
CD4
gp120
T4 LYMPHOCYTE
F
DP-107
DP-178
VIRUS MEMBRANE
FUSOGENIC
NATIVE

FIG.11B

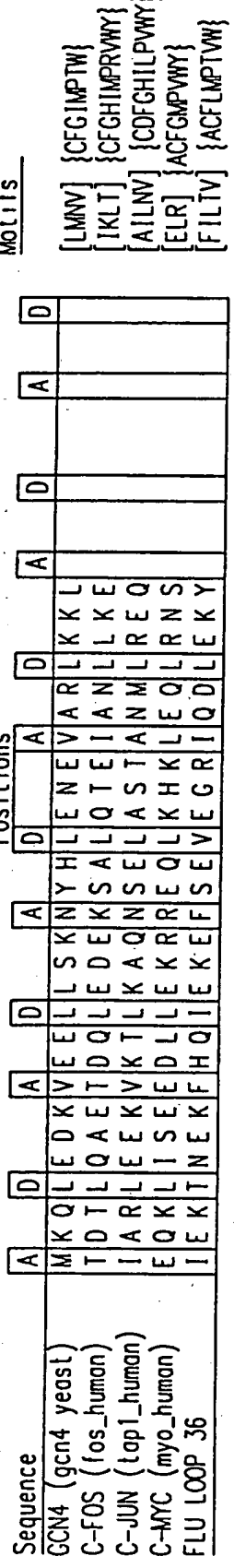
Positions
Motifs
Sequence
GCN4 (gcn4 yeast)
C-FOS (fos_human)
C-JUN (jap1_human)
C-MYC (myo_human)
FLU LOOP 36
[LMNV] {CFGIMPTW}
[IKLT] {CFGHIMPRVWY}
[AILNV] {CDFGHILPVWY}
[ELR] {ACFGMPVWY}
[FILTV] {ACFLMPTVW}

FIG.12

Positions
Sequence
Motifs
DP-107 (env_hv1bru)L1=D [ILQT] {CFIMPSTY}
DP-107 (env_hv1bru)L1=D [ILQTV] {CDFIMPST}
DP-107 (env_hv1bru)L1=D [ILQTV] {CDFIMPST}
DP-107 (env_hv1bru)L2=D [EKLNQV] {CDFKMPSVY}
DP-107 (env_hv1bru)L2=D [EKLNQV] {CFKMPS}
DP-107 (env_hv1bru)L2=D [EKLNQV] {CFKMPS}
DP-178 (env_hv1bru)Y1=A [EKLQY] {ACFGMPRVWY}
DP-178 (env_hv1bru)Y1=A [EKLQWY] {CFGMPRVY}
DP-178 (env_hv1bru)Y1=A [EFKLQWY] {CFGMPRVY}
DP-178 (env_hv1bru)Y1=D [EILNQSY] {ACFGMPRVWY}
DP-178 (env_hv1bru)Y1=D [EILNQSWY] {CFGMPRVY}
DP-178 (env_hv1bru)Y1=D [EFILNQSWY] {CFGMPRVY}

FIG.13

Sequence	Positions																															Parent Motif	Hybrid Motif
	A		D			A		D				D		A		D			A		D												
GCN4 (gcn4 yeast)	M	K	Q	L	E	D	K	V	E	E	L	L	S	K	N	Y	H	L	E	N	E	V	A	R	L	K	K	L				[LMNV]	[CFGIMPTW]
DP-107 (env_hv1bru)L1=0	N	N	L	L	R	A	I	E	A	Q	Q	H	L	L	Q	L	T	V	W	G	I	K	Q	L	Q	A	R	I				[ILQT]	[CFIMPSTY]	[ILMNQTV]	[CFIMPT]
DP-107 (env_hv1bru)L1=0	N	N	L	L	R	A	I	E	A	Q	Q	H	L	L	Q	L	T	V	W	G	I	K	Q	L	Q	A	R	I	L	A	V	[ILQTV]	[CDFIMPST]	[ILMNQTV]	[CFIMPT]
DP-107 (env_hv1bru)L1=0	N	N	L	L	R	A	I	E	A	Q	Q	H	L	L	Q	L	T	V	W	G	I	K	Q	L	Q	A	R	I	L	A	V	[ILQTV]	[CDFIMPST]	[ILMNQTV]	[CFIMPT]
DP-107 (env_hv1bru)L2=0	N	N	L	L	R	A	I	E	A	Q	Q	H	L	L	Q	L	T	V	W	G	I	K	Q	L	Q	A	R	I				[EKLNQV]	[CDFKMPSVY]	[EKLMNQV]	[CFMP]
DP-107 (env_hv1bru)L2=0	N	N	L	L	R	A	I	E	A	Q	Q	H	L	L	Q	L	T	V	W	G	I	K	Q	L	Q	A	R	I	L	A	V	[EKLNQV]	[CFKMPS]	[EKLMNQV]	[CFMP]
DP-107 (env_hv1bru)L2=0	N	N	L	L	R	A	I	E	A	Q	Q	H	L	L	Q	L	T	V	W	G	I	K	Q	L	Q	A	R	I	L	A	V	[EKLNQV]	[CFKMPS]	[EKLMNQV]	[CFMP]

FIG.14

Sequence	Positions																											Parent Motif	Hybrid Motif
	A		D			A		D			A		D				A		D				A		D				
GCN4 (gcn4 yeast)	M	K	Q	L	E	D	K	V	E	E	L	L	S	K	N	Y	H	L	E	N	E	V	A	R	L	K	K	L			[LMNV] {CFG1MPTW}	
DP-178 (env_hv1bru)Y1=A	Y	T	S	L	I	I	H	S	L	I	E	E	S	Q	N	Q	Q	E	K	N	E	Q	E	L	L	E	L	D	K				[EKLQY] {ACFGMPRVWY}	[EKLMNQVY] {CFGMPW}
DP-178 (env_hv1bru)Y1=A	Y	T	S	L	I	I	H	S	L	I	E	E	S	Q	N	Q	Q	E	K	N	E	Q	E	L	L	E	L	D	K	W	A	S	L	[EKLMNQWY] {CFGMP}	
DP-178 (env_hv1bru)Y1=A	Y	T	S	L	I	I	H	S	L	I	E	E	S	Q	N	Q	Q	E	K	N	E	Q	E	L	L	E	L	D	K	W	A	S	L	W	N	W	[EFKLQWY] {CFGMPRVY}	[EFKLMNQVWY] {CFGMP}
DP-178 (env_hv1bru)Y1=D				Y	T	S	L	I	H	S	L	I	E	E	S	Q	N	Q	Q	E	K	N	E	Q	E	L	L	E	L	D	K				[EILNQSY] {ACFGMPRVWY}	[EILMNQSVY] {CFGMPW}
DP-178 (env_hv1bru)Y1=D				Y	T	S	L	I	H	S	L	I	E	E	S	Q	N	Q	Q	E	K	N	E	Q	E	L	L	E	L	D	K	W	A	S	L	W	N	W	[EILNQSWY] {CFGMPRVY}	[EILMNQSVWY] {CFGMP}
DP-178 (env_hv1bru)Y1=D				Y	T	S	L	I	H	S	L	I	E	E	S	Q	N	Q	Q	E	K	N	E	Q	E	L	L	E	L	D	K	W	A	S	L	W	N	W	F	[EFILNQSWY] {CFGMPRVY}	[EFILMNQSVWY] {CFGMP}

FIG.15

Sequence	Positions																															Parent Motif	Hybrid Motif
	A		D			A		D			A		D			A		D			A		D			A		D				
DP-107 (env_hv1bru)L1=D		N	N	L	L	R	A	I	E	A	Q	Q	H	L	L	Q	L	T	V	W	G	I	K	Q	L	Q	A	R	I	L	A	V	E	R	Y	L	K	D	Q	[ILQTV] {CDFIMPST}	
DP-107 (env_hv1bru)L2=D		N	N	L	L	R	A	I	E	A	Q	Q	H	L	L	Q	L	T	V	W	G	I	K	Q	L	Q	A	R	I	L	A	V	E	R	Y	L	K	D	Q	[EKLNQV] {CFKMPS}	
DP-178 (env_hv1bru)Y1=A		Y	T	S	L	I	H	S	L	I	E	E	S	Q	N	Q	Q	E	K	N	E	Q	E	L	L	E	L	D	K	W	A	S	L	W	N	W	F			[EFKLQWY] {CFGMPRVY}	
DP-178 (env_hv1bru)Y1=D			Y	T	S	L	I	H	S	L	I	E	E	S	Q	N	Q	Q	E	K	N	E	Q	E	L	L	E	L	D	K	W	A	S	L	W	N	W	F			[EFILNQSWY] {CFGMPRVY}	[EFIKLMQSTVWY] {CFMP}
FLU LOOP 36		I	E	K	T	N	E	K	F	H	Q	I	E	K	E	F	S	E	V	E	G	R	I	Q	D	L	E	K	Y												[FILTV] {ACFLMPTVW}	

FIG.16

Sequence	Positions	Parent Motif	Hybrid Motif
GCN4 (gcn4 yeast)	M K Q L E D K V E E L L S K N Y H L E N E V A R L K K L	[LMNV] {CFGIMPTW}	
DP-107 (env_hv1bru)L1=D	N N L L R A I E A Q Q H L L Q L T V W G I K Q L Q A R I L A V E R Y L K D Q	[ILQTV] {CDFIMPST}	
DP-178 (env_hv1bru)Y1=A	Y T S L I M S L I E E S Q N Q Q E K N E Q E L L E L D K W A S L W N W F	[EFKLQWY] {CFGMPRVY}	[EFIKLMNQTVWY] {CFMP}
GCN4 (gcn4 yeast)	M K Q L E D K V E E L L S K N Y H L E N E V A R L K K L	[LMNV] {CFGIMPTW}	
DP-107 (env_hv1bru)L1=D	N N L L R A I E A Q Q H L L Q L T V W G I K Q L Q A R I L A V E R Y L K D Q	[ILQTV] {CDFIMPST}	
DP-178 (env_hv1bru)Y1=D	Y T S L I H S L I E E S Q N Q Q E K N E Q E L L E L D K W A S L W N W F	[EFILNQSWY] {CFGMPRVY}	[EFILMNQRSTVWY] {CFMP}
GCN4 (gcn4 yeast)	M K Q L E D K V E E L L S K N Y H L E N E V A R L K K L	[LMNV] {CFGIMPTW}	
DP-107 (env_hv1bru)L2=D	N N L L R A I E A Q Q H L L Q L T V W G I K Q L Q A R I L A V E R Y L K D Q	[EKLNQV] {CFKMPS}	
DP-178 (env_hv1bru)Y1=A	Y T S L I H S L I E E S Q N Q Q E K N E Q E L L E L D K W A S L W N W F	[EFKLQWY] {CFGMPRVY}	[EFKLMNQVWY] {CFMP}
GCN4 (gcn4 yeast)	M K Q L E D K V E E L L S K N Y H L E N E V A R L K K L	[LMNV] {CFGIMPTW}	
DP-107 (env_hv1bru)L2=D	N N L L R A I E A Q Q H L L Q L T V W G I K Q L Q A R I L A V E R Y L K D Q	[EKLNQV] {CFKMPS}	
DP-178 (env_hv1bru)Y1=D	Y T S L I H S L I E E S Q N Q Q E K N E Q E L L E L D K W A S L W N W F	[EFILNQSWY] {CFGMPRVY}	[EFIKLMNQSVWY] {CFMP}

FIG.17

Positions
Sequence
GCN4 (gcn4_yeast)
DP-107 (env_hv1bru)L1=D
DP-107 (env_hv1bru)L2=D
DP-178 (env_hv1bru)Y1=A
DP-178 (env_hv1bru)Y1=D
C-FOS (fos_human)
C-JUN (jap1_human)
C-MYC (myo_human)
FLU LOOP 36
Parent Motif
[LMNV] {CFGIMPTW}
[ILQTV] {CDFIMPST}
[EKLNQV] {CFKMPS}
[EFKLQWY] {CFGMPRVY}
[EFILNQSWY] {CFGMPRVY}
[IKLT] {CFGHIMPRVWY}
[AILNV] {CDFGHILPVWY}
[ELR] {ACFGMPVWY}
[FILTV] {ACFLMPTVW}
Hybrid Motif
[ACFIKLMNQRSTVWY] {CFP}
= {CDGHP} {CFP}

FIG.18

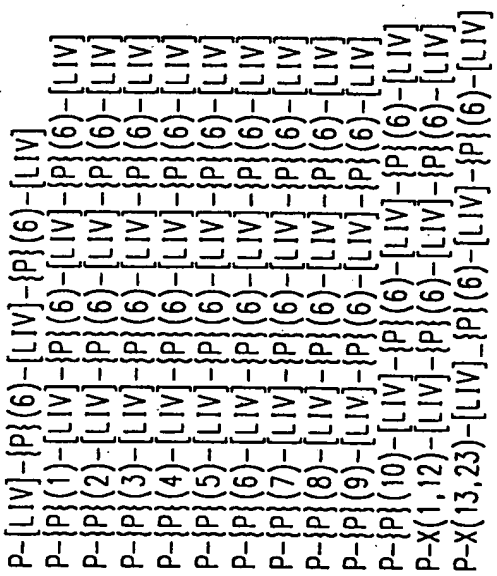
P-[LIV]-{P}(6)-[LIV]-{P}(6)-[LIV]
P-{P}(1)-[LIV]-{P}(6)-[LIV]-{P}(6)-[LIV]
P-{P}(2)-[LIV]-{P}(6)-[LIV]-{P}(6)-[LIV]
P-{P}(3)-[LIV]-{P}(6)-[LIV]-{P}(6)-[LIV]
P-{P}(4)-[LIV]-{P}(6)-[LIV]-{P}(6)-[LIV]
P-{P}(5)-[LIV]-{P}(6)-[LIV]-{P}(6)-[LIV]
P-{P}(6)-[LIV]-{P}(6)-[LIV]-{P}(6)-[LIV]
P-{P}(7)-[LIV]-{P}(6)-[LIV]-{P}(6)-[LIV]
P-{P}(8)-[LIV]-{P}(6)-[LIV]-{P}(6)-[LIV]
P-{P}(9)-[LIV]-{P}(6)-[LIV]-{P}(6)-[LIV]
P-{P}(10)-[LIV]-{P}(6)-[LIV]-{P}(6)-[LIV]
P-X(1,12)-[LIV]-{P}(6)-[LIV]-{P}(6)-[LIV]
P-X(13,23)-[LIV]-{P}(6)-[LIV]-{P}(6)-[LIV]

FIG.19

Fusion ♥ALLMOTI5♥
Peptide
♠107x178x4♠
♥.....FLGFLG A AGSTMGARSM TLTVQARQ ♠LL SGIVQQQ *DP107-NNL*

LRAIEAQQHL LQLTVWGIKQ LQARILAVER YLKDQ-DP107 QLLG♠♥ I WGC

♠107x178x4♠
♥ALLMOTI5♥ *LVS Coiled-Coil*
SGKLICT TAVP ♥WNASWS NKSLEQIWNN MTWM *E ♠WDREI NN *DP178-*

YTSLIHSL IEESQNQQEK NEQELLELDK WASLWNWF-DP178* NI

♦Transmembrane Region♦
TNWLWYIK♠ ♦IF IMIVGGLVGL RIVFAVLSIV NRVRQGYS♥ PL

♣P23LZIPC♣
SFQTHLPTPR GPDR ♣PEGIEE EGGERDRDRS IRLVNGSLAL IWDDLRSL♣ CL

♥ALLMOTI5♥ ♠107x178x4♠
F ♥SYHRLRDLL LIVTRIVELL GRRGW ♠EALKY WWNLLQYWSQ

ELKNSAVSLL NAT♠ AIAVAEG TDRVIEVVQG A♥ CRAIRHIPR

RIRQGLERIL L

FIG. 20

Fusion ♥ALLMOTI5♥
Peptide ♠107x178x4♠
♥.....FLGFL LGVGSAIAS GVA ♠VSKVLHL EGEVNKIKSA

♣P1&12LZIPC♣
LLSTNKAVVS LSNGVSVLTS KVLDLKNYID KQ♠♥ LL ♣PIVNKQ

♠107x178x4♠
SC ♠SISNIETV I♣ EFQQKNNRLLEITREFSVNAG♠ VTTPVSTMLTNSELLSL

♣P1&12LZIPC♣
♥ALLMOTI5♥
INDM ♣PI ♥TNDQ KKLMSNNVQI V♣ RQQSYSI♣ MS IIKEEVLAYV

VQ♥ LPLYGVID TPCWKLHTSP LCTTNTKEGS NICLTRTDRG WYCDNAGSVS

FFPQAETCKV QSNRVFCDTM NSLTLPSEIN LCNVDIFNPK

YDCKIMTSKT DVSSSVITSL GAIVSCYGKT KCTASNKNRG

IIKTFSNGCDYVSNKGMDTV SVGNTLYYVN KQEGKSLYVK G

♣P7, 12, & 23LZIPC♣
♠107x178x4♠ ♥ALLMOTI5♥
EPIINFYDPLVF ♣PSDE ♠FDASISQVNEKINQSLAF ♥I♣ RKSDELL♣

♦Transmembrane Region♦
HNVNA♠ GK STTN ♦IMITTI IIVIIVILLS LIAVGLLLY♥ C♦

KARSTPVTLS KDQLSGINNI AFSN

FIG. 21

Fusion
Peptide ♥ALLMOTI5♥ ♠107x178x4♠
.....FLGFLG ♥AAGTA MGAAA ♠TALTVQSQHLLAGILQQQKNLLAAV

♠107x178x4♠
EAQ♠ QQM ♠LKLTIWGVKNLNARVTALEKYLEDQARLN♠ AWG♥ CA

LVS Coiled-Coil
♥ALLMOTI5♥ ♠107x178x4♠
WKQVCHTTVP WQWNNRTPDW ♥NNMT *WLE ♠WERQISYLEGNIT

♠107x178x4♠
TQLEEARAQEEKNLD♠ AYQKLSS* WSDFWSW♥ FDF ♠SKWLN ♦ILK

♦Transmembrane Region♦
IGFLDVLGIIGLRLLYTV♦ YS♠ CIARVRQGYS PLSPQIHIHP WKGQPDNAEG

PGEGGDKRKN SSEPWQKESG TAEWKSNWCK RLTNWCSISS IWLYNS

♥ALLMOTI5♥
♥CLTL LVHLRSAFQY IQYGLGELKA AAQEAVVALA RLAQNAGYQIWL♥

ACRSAYRA IINSPRRVRQ GLEGILN

FIG. 22

Fusion Peptide .....FAG ♥ALLMOTI5♥ ♥VVL AGVALGVATA AQITAGIALHQ ♠107x178x4♠ *LVS Coiled-Coil* ♠*SNLNAQAIQ

SLRTSLEQSNKAIEEIREATQETVIA* VQGVQDY♠ VNNEL♥ VP

♥ALLMOTI5♥
♠107x178x4♠
♣P6 & 12LZIPC♣
AMQHMSCELVGQRLGLRLLRYYTELLSIFGPSLRD ♣PISA ♠♥EISIQALIYAL

GGEIIHKILEKLGYSGSD♠ MIAILESRGIKTKI♥ THVDLPGKF IILSISY

♣P1 & 12LZIPC♣
♣PTLSEVKGVIVHRLEAV♣ SYNIGSQEWYTTVPRYIATNGYLISNFDESSCVFVS

ESAICSQNSL YPMSPLLQQC IRGDTSSCAR TLVSGTMGNK FILSKGNIVA

NCASILCKCY STSTIINQSP DKLLTFIASD TCPLVEIDGA TIQVGGRQYP

LVS Coiled-Coil
♥ALLMOTI5♥
♣P12 & 23LZIPC♣
DMVYEGKVAL G ♣PAISLD ♥RL*DVGTNLGNALKKLDDAKVLI♣

♦Transmembrane Region♦
DSS♣ NQILETVR RS♥* SFN ♦FGSLL SVPILSCTAL ALLLLIYCC♦

K RRYQQTLKQH TKVDPAFKPD LTGTSKSYVR SL

FIG. 23

Fusion ♥ALLMOTI5♥
Peptide
♠107x178x4♠
♥.....FIGAI IGSVALGVA TAAQITAASA LIQANQNAAN ♠ILRLKESITA

TIEAVHEVTDGLSQLAVA♠ VG KM♥ QQFVNDQFNNTAQELDCIKITQQV

♥ALLMOTI5♥
GVELNLYLTELTTV FGPQITSPAL ♥TQLTIQALYNAGGNMDYLLTKLGVG

♣P1 & 12LZIPC♣
NNQLSSLIGSGLIT GN♥ ♣PILYDSQT QLLGIQVTLP SVGNLNNMRATYLET

LSVST TKGFASALVP KVVTQVGSVI EELDTSYCIE TDLDLYCTRI VTFPMSPGIY

SCLNGNTSAC MYSKTEGALT TPYMTLKGSV IANCKMTTCR CADPPGIISQ

♥ALLMOTI5♥
♠107x178x4♠
NYGEAVSLID RHSCN ♠♥VLSLD GITLRLSGEF DATYQKNISI LDSQVIVTG

LVS Coiled-Coil ♦Trans-
N LDISTELGNV NNSISNALDK LEESNSKLDK VNVKLTSTSA ♦LIT YIA

membrane Region♦
LTAISLVCGILSLV♥♠ LACYLMY♦ KQKAQQKTLLWLGNNTLGQMRATTKM

FIG. 24

Fusion ♥ALLMOTI5♥
Peptide ♠107x178x4♠ *LVS Coiled-Coil*
.....FFGGV ♠IG ♥TIALG *VATSAQITAAVALVEAKQARSDIEKLKE

AIRDTNKAVQSVQSSIGNLIVAIKSVQ* DYVNKE♥♠ IVPSIARLGCEAAG

♥ALLMOTI5♥
♠107x178x4♠
LQLGIALTQH ♠♥YSELTNIFGDNIGSLQEKGIKLQGIASLYRTNITE♥♠

♣P5 & 12LZIPC♣
IFTTSTVDKYDIYDLLFTESIKVRVIDVDLNDYSITLQVRL ♣PLLTRLLNTQIYR

VDSISYNI♣ QNREWYI♣ PLPSHIMTKGAFLGGADVKECIEAFSSYIC

PSDPGFVLNHEMESCLSGNISQCPRTVVKSDIVPRYAFVNGGVVANCITT

TCTCNGIGNRINQPPDQGVKIITHKECNTIGINGMLFNTNKEGTLAFYTP

♥ALLMOTI5♥
♠107x178x4♠
♣P6 & 23LZIPC♣
NDITLNNSVALD ♣PIDI ♠SIELN ♥KAKSDLEESKEWI♣ RRSNQKL♣

♦Transmembrane Region♦
DSIGNWHQSSTT ♦IIIV♠ LIM IIILFIINVT II♦ IIAVKYY♥ R

IQKRNRVDQN DKPYVLTNK

FIG. 25

Fusion
Peptide
.....GLFGAI AGFIENGWEGMIDGWYGFRHQNSEGTG

♠107x178x4♠
♥ALLMOTI5♥
LVS Coiled-Coil
*Q ♥AADLKST ♠QAAIDQINGKLNRVIEKTNEKFHQIEKEFSEVEGRIQ

DLEKYVEDTKIDL* WSYNAELLVALENQHTI♠ DLT♥ DSEMNKLFEKTR

RQLRENAEEMGNGCFKIYHKCDNACIESIRNGTYDHDVYRDEALNNRFQIKG

VELKSGYKDWILWISFAISCFLLCVVLLGFIMWACQRGNIRCNICI

FIG. 26

AV	CD	RSV F2	
+	+/++	T-142	YTSVITIELSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST
++	+/+++	T-143	YTSVITIELSNIKENKCNGTDAKVKLIKQELDKYK
+	+/++	T-144	TSVITIELSNIKENKCNGTDAKVKLIKQELDKYKN
-	+/+	T-145	SVITIELSNIKENKCNGTDAKVKLIKQELDKYKNA
-	+/-	T-146	VITIELSNIKENKCNGTDAKVKLIKQELDKYKNAV
-		T-147	ITIELSNIKENKCNGTDAKVKLIKQELDKYKNAVT
-	-	T-148	TIELSNIKENKCNGTDAKVKLIKQELDKYKNAVTE
-	+/-	T-149	IELSNIKENKCNGTDAKVKLIKQELDKYKNAVTEL
-	-	T-150	ELSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQ
-	+/+	T-151	LSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQL
-	+/++	T-152	SNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLL
-	+/+	T-153	NIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLM
-	+/++	T-154	IKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQ
-	+/+	T-155	KENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQS
			ENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST

FIG.27

AV	CD	RSV	
++	+/-	T-67	DEFDASISQVNEKINQSLAFIRKSDELL
		F1-178	GEPIINFYDPLVFPSDEFDASISQVNEKINQSLAFIRKSDELLHNVNAGKSTT
+/-		T-104	IINFYDPLVFPSDEFDASISQVNEKINQSLAFIRK
+/-		T-105	INFYDPLVFPSDEFDASISQVNEKINQSLAFIRKS
+/-		T-106	NFYDPLVFPSDEFDASISQVNEKINQSLAFIRKSD
+		T-107	FYDPLVFPSDEFDASISQVNEKINQSLAFIRKSDE
++		T-108	YDPLVFPSDEFDASISQVNEKINQSLAFIRKSDEL
++		T-109	DPLVFPSDEFDASISQVNEKINQSLAFIRKSDELL
+		T-110	PLVFPSDEFDASISQVNEKINQSLAFIRKSDELLH
++		T-111	LVFPSDEFDASISQVNEKINQSLAFIRKSDELLHN
++	+/-	T-112	VFPSDEFDASISQVNEKINQSLAFIRKSDELLHNV
++	+/-	T-113	FPSDEFDASISQVNEKINQSLAFIRKSDELLHNVN
++	+/-	T-114	PSDEFDASISQVNEKINQSLAFIRKSDELLHNVNA
++	+/-	T-115	SDEFDASISQVNEKINQSLAFIRKSDELLHNVNAG
++	+/-	T-116 (T-67 LIKE)	DEFDASISQVNEKINQSLAFIRKSDELLHNVNAGK
++	+/-	T-117	EFDASISQVNEKINQSLAFIRKSDELLHNVNAGKS
++	+/-	T-118	FDASISQVNEKINQSLAFIRKSDELLHNVNAGKST
++	+/-	T-119	DASISQVNEKINQSLAFIRKSDELLHNVNAGKSTT

FIG.28

AV	CD	HPF3 178	YTPNDITLNNSVALDPIDISIELNKAKSDLEESKEWIRRSNQKLDSIGNWHQSSTT
-	-	189	YTPNDITLNNSVALDPIDISIELNKAKSDLEESKE
-	-	190	TPNDITLNNSVALDPIDISIELNKAKSDLEESKEW
-	-	191	PNDITLNNSVALDPIDISIELNKAKSDLEESKEWI
-	-	192	NDITLNNSVALDPIDISIELNKAKSDLEESKEWIR
-	+/-	193	DITLNNSVALDPIDISIELNKAKSDLEESKEWIRR
+/-	+/-	194	ITLNNSVALDPIDISIELNKAKSDLEESKEWIRRS
+/-	+/+ +	195	TLNNSVALDPIDISIELNKAKSDLEESKEWIRRSN
+	+/+	196	LNNSVALDPIDISIELNKAKSDLEESKEWIRRSNQ
+	+/+	197	NNSVALDPIDISIELNKAKSDLEESKEWIRRSNQK
+++	+/+	198	NSVALDPIDISIELNKAKSDLEESKEWIRRSNQKL
++	+/+	199	SVALDPIDISIELNKAKSDLEESKEWIRRSNQKLD
-		200	VALDPIDISIELNKAKSDLEESKEWIRRSNQKLDS
+++		201	ALDPIDISIELNKAKSDLEESKEWIRRSNQKLDSI
+++		202	LDPIDISIELNKAKSDLEESKEWIRRSNQKLDSIG
++		203	DPIDISIELNKAKSDLEESKEWIRRSNQKLDSIGN
++		204	PIDISIELNKAKSDLEESKEWIRRSNQKLDSIGNW
+++		205	IDISIELNKAKSDLEESKEWIRRSNQKLDSIGNWH
+		206	DISIELNKAKSDLEESKEWIRRSNQKLDSIGNWHQ
+		207	ISIELNKAKSDLEESKEWIRRSNQKLDSIGNWHQS
+		208	SIELNKAKSDLEESKEWIRRSNQKLDSIGNWHQSS
++		209	IELNKAKSDLEESKEWIRRSNQKLDSIGNWHQSST
++		210	ELNKAKSDLEESKEWIRRSNQKLDSIGNWHQSSTT

FIG.29

CD	HPF3	107
		GTIALGVATSAQITAAVALVEAKQARSDIEKLKEAIRDTNKAVQSVQSSIGNLIVAIKSVQDYVNKEIVP
+/+	157	ALGVATSAQITAAVALVEAKQARSDIEKLKEAIRD
+/+	158	LGVATSAQITAAVALVEAKQARSDIEKLKEAIRDT
+/-	159	GVATSAQITAAVALVEAKQARSDIEKLKEAIRDTN
+/+	160	VATSAQITAAVALVEAKQARSDIEKLKEAIRDTNK
+/+	161	ATSAQITAAVALVEAKQARSDIEKLKEAIRDTNKA
+/-	162	TSAQITAAVALVEAKQARSDIEKLKEAIRDTNKAV
+/+	163	SAQITAAVALVEAKQARSDIEKLKEAIRDTNKAVQ
+/+++	164	AQITAAVALVEAKQARSDIEKLKEAIRDTNKAVQS
+/+	165	QITAAVALVEAKQARSDIEKLKEAIRDTNKAVQSV
+/-	166	ITAAVALVEAKQARSDIEKLKEAIRDTNKAVQSVQ
+/-	167	TAAVALVEAKQARSDIEKLKEAIRDTNKAVQSVQS
+/-	168	AAVALVEAKQARSDIEKLKEAIRDTNKAVQSVQSS
+/-	169	AVALVEAKQARSDIEKLKEAIRDTNKAVQSVQSSI
+/-	170	VALVEAKQARSDIEKLKEAIRDTNKAVQSVQSSIG
+/-	171	ALVEAKQARSDIEKLKEAIRDTNKAVQSVQSSIGN
+/-	172	LVEAKQARSDIEKLKEAIRDTNKAVQSVQSSIGNL
+/-	173	VEAKQARSDIEKLKEAIRDTNKAVQSVQSSIGNLI
+/++	174	EAKQARSDIEKLKEAIRDTNKAVQSVQSSIGNLIV
	T-40	AKQARSDIEKLKEAIRDTNKAVQSVQSSIGNLIVA
+/++	175	KQARSDIEKLKEAIRDTNKAVQSVQSSIGNLIVAI
+/+++	176	QARSDIEKLKEAIRDTNKAVQSVQSSIGNLIVAIK
+/-	177	ARSDIEKLKEAIRDTNKAVQSVQSSIGNLIVAIKS
+/-	178	RSDIEKLKEAIRDTNKAVQSVQSSIGNLIVAIKSV
-	179	SDIEKLKEAIRDTNKAVQSVQSSIGNLIVAIKSVQ
-	180	DIEKLKEAIRDTNKAVQSVQSSIGNLIVAIKSVQD
-	181	IEKLKEAIRDTNKAVQSVQSSIGNLIVAIKSVQDY
-	182	EKLKEAIRDTNKAVQSVQSSIGNLIVAIKSVQDYV
+/++	183	KLKEAIRDTNKAVQSVQSSIGNLIVAIKSVQDYVN
+/+++	184	LKEAIRDTNKAVQSVQSSIGNLIVAIKSVQDYVNK
-	185	KEAIRDTNKAVQSVQSSIGNLIVAIKSVQDYVNKE
-	186	EAIRDTNKAVQSVQSSIGNLIVAIKSVQDYVNKEI
-	187	AIRDTNKAVQSVQSSIGNLIVAIKSVQDYVNKEIV
-	188	IRDTNKAVQSVQSSIGNLIVAIKSVQDYVNKEIVP

FIG.30

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US94/05739

A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) : A61K 37/02, 39/12; C12Q 1/70; G01N 33/53

US CL : 424/88, 89; 435/5, 7.1, 7.92-7.95, 974; 530/324-331, 333, 334

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/88, 89; 435/5, 7.1, 7.92-7.95, 974; 530/324-331, 333, 334

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS, Biosis

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
NONE	NONE	NONE

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
07 SEPTEMBER 1994	26 SEP 1994

Name and mailing address of the ISA/US	Authorized officer
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Form PCT/ISA/210 (second sheet)(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US94/05739

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 2
because they relate to subject matter not required to be searched by this Authority, namely:

that the claimed subject matter is directed to mental processes.

2. [X] Claims Nos.: 13-16 and 42-49
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

because the sequences have not been submitted to the International Searching Authority in electronic form.

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.